UNITED STATES DISTRICT COURT
DISTRICT OF NEW JERSEY

IN RE: JOHNSON & JOHNSON TALCUM POWDER PRODUCTS MARKETING, SALES PRACTICES, AND PRODUCTS LIABILITY LITIGATION	**MDL No. 16-2738 (MAS) (RLS)**
THIS DOCUMENT RELATES TO ALL CASES	

THE PLAINTIFFS' STEERING COMMITTEE'S MEMORANDUM OF LAW IN OPPOSITION TO DEFENDANTS' MOTION TO EXCLUDE PLANTIFFS' EXPERTS' GENERAL CAUSATION OPINIONS

TABLE OF CONTENTS

INTRODUCTION 1
BACKGROUND 6
I. Chief Judge Wolfson's 2020 *Daubert* ruling. 6
A. The state of the scientific record in 2020. 7
B. Judge Wolfson's 2019 *Daubert* hearing and 2020 *Daubert* ruling. 14
II. The scientific and regulatory record after 2020. 20
A. It is now generally accepted that talcum powders contain asbestos. 21
B. There are important new cohort studies that support a causal association between talcum powder and ovarian cancer. 24
1. O'Brien 2020 25
2. O'Brien 2024 28
3. Woolen 2022 31
4. Chang 2024 31
5. Davis 2021 32
C. Regulatory authorities and professional organizations have now found a causal association between talcum powders—with and without asbestos—and ovarian cancer. 33
III. Plaintiffs' expert witnesses, their opinions, and their methodologies. 38
A. Anne McTiernan, MD, PhD 39
B. Jack Siemiatycki, MSc, PhD 43
C. Rebecca Smith-Bindman, MD 45
D. Bernard J. Harlow, PhD 47
E. Michele L. Cote, Ph.D., M.P.H. 50
F. Sonal Singh, PhD 52
G. Patricia Moorman, MSPH, PhD 54
H. Daniel Clarke-Pearson, MD 56
I. Judith Wolf, MD 58
ARGUMENT 61

IV. J&J's arguments stemming from the Rule 702 amendments in 2023 are baseless. 61

A. J&J seeks what the Court already refused to consider: to have Judge Wolfson's work thrown away and redone. 61

B. Rule 702 was amended in 2023, but the amendment was not intended to change the law or upset decades of settled practice. 63

C. Judge Wolfson followed Rule 702 as it was written then and her decision is no less correct under today's Rule 702. 64

V. The new science post-2020 strengthens Plaintiffs' experts' opinions. 67

A. Strength of association: New post-2020 study evidence further supports the strength of the association. 71

1. J&J must now accept that there is strong and consistent epidemiological data from multiple study designs.....73

2. J&J again attempts to disclaim the evidence as methodologically "weak," which Judge Wolfson already rejected. 73

3. A 2.0 increased risk ratio is not necessary to find causation.....76

4. Plaintiffs' experts considered recall bias and confounders. 77

B. Consistency of association: New post-2020 cohort study evidence supports a finding of consistency among all the studies 78

1. The post-2020 "new science" confirms a consistent association among the case-control studies, meta-analyses, and cohort studies. 80

2. J&J's renewed *Daubert* challenge rests on the discredited view of "significance testing" already addressed by Judge Wolfson; a view rejected by the American Statistical Association (ASA), and which is described in the *Reference Manual* as unsophisticated. 82

3. It is J&J and its causation experts, not Plaintiffs' causation experts, who ignore statistical significance in the post-2024 talcum powder studies. ..89

C. Dose-response relationship: New post-2020 cohort study evidence strengthens this finding, while J&J has no new scientific evidence to the contrary. 90

D. Biological plausibility: post-2020 evidence further strengthens this factor. 93

CONCLUSION.....95

TABLE OF AUTHORITIES

Cases

Brower, et al. v *Johnson & Johnson, et al.*, No. 16-EV-5534-E (Ga. Super. Ct.–Fulton County) (Mar. 26, 2019) 18

Carl v. Johnson & Johnson, No. ATL-L-6456-14, 2016 WL 4580145 (N.J. Super Ct. Law Div. Sept. 2, 2016) 19

Daniels, et al. v. Johnson & Johnson, et al., No. 1422-CC09326-01 (City of St. Louis, MO) (Feb. 6, 2017) 18

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Daubert v. Merrell Dow Pharms, Inc., 509 U.S. 579 (1993) ..... passim

Echeverria, et al. v. Johnson & Johnson, et al., No. BC628228, JCCP No. 4872 (Cal. Super. Ct. 2017) 18

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In re Processed Egg Prods. Antitrust Litig., 81 F. Supp. 3d 412, 416 (E.D. Pa. 2015) 65

In re Roundup Prods. Liab. Litig., 390 F. Supp. 3d 1102, 1130 (N.D. Cal. 2018) .. 65

In re TMI Litig. Cases Consol. II, 922 F. Supp. 997, 1017 (M.D. Pa. 1996) 87

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National Academies of Science, Engineering and Medicine, *Ovarian* 6

NIH/NIEHS Environmental Factor, *Genital talc use may be linked to increase risk of ovarian cancer* (June 2024) 5, 70, 81

O'Brien 2020..... 25, 26

O'Brien et al., *Association of Powder Use in the Genital Area with Risk of Ovarian Cancer*, 323 JAMA 49 (2020) 3, 69, 93

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Rules

Fed. R. Evid. 702 ..... passim

Treatises

Federal Judicial Center, *Reference Manual on Scientific Evidence*, (3d ed. 2011) ..... passim

Rothman, et al., *Modern Epidemiology* (3d ed. 2009)..... 8, 74, 84

Regulations

86 Fed. Reg. 74088 (Dec. 19, 2021).....22

88 Fed. Reg. 47782 (July 25, 2023)..... 5, 22, 35

89 Fed. Reg. 21970 .....5, 35

INTRODUCTION

The PSC opposes Defendants' motion to exclude Plaintiffs' experts' general causation opinions.

This round of *Daubert* challenges was not intended to be a duplication of the prior work in this MDL. In ordering this briefing on April 30, 2024, the Court informed the parties that it would not "*sua sponte* thr[o]w away Chief Judge Wolfson's findings" and did not "intend [] to start *Daubert* motions over from scratch." (ECF No. 32122 at 3.) And the Court directed the parties to "identify either: (1) that Chief Judge Wolfson's previous Opinion demonstrably fails to adhere to Rule 702 as clarified by the 2023 amendments; or (2) new science is shown to directly contradict or challenge Chief Judge Wolfson's previous findings."

In bringing this motion, J&J apparently did not see eye-to-eye with the Court. J&J's motion goes well outside the scope of the Court's Order, to challenge the validity of the scientific evidence and scientific methodology on which the PSC's slate of experts rely. In 2020, Judge Wolfson carefully considered these same challenges before—and rejected them. The Court should do so again.

When it focuses on what actually *is* new since 2020, Plaintiffs believe the Court will reach two conclusions:

First, that Judge Wolfson's opinion is not undercut by the changes to Rule 702 in 2023—because those changes were minor and only clarified the existing standard. Judge Wolfson's opinion rests on the same solid foundation today as in 2020.

J&J wrongly claims that the change to Rule 702 was somehow sweeping, "which explains why significant swaths of [Judge Wolfson's] ruling misapprehend the pertinent legal standard." (Mem. at 33.) And—in a pretty thin argument grounded on not much more than a mechanical word count—J&J claims that whole swaths of that settled, published opinion were undercut by the change to the Rule.

As will be examined, this is nonsense. The Rule was not dramatically changed. Federal courts have been steadily elaborating and applying the *Daubert* principles since *Daubert itself* was decided in the 1990s. Yes, Rule 702 was amended last year, but it was to clarify and better codify the ongoing practice—which Judge Wolfson followed. Plaintiffs will discuss why the Rule was amended and what the amendment's drafters themselves said about their work.

And second, the scientific record that fully supported Judge Wolfson's 2020 decision to admit Plaintiffs' general causation experts has only developed since 2020—and that scientific record has become stronger.

Science marches on. The scientific academy has continued to examine the question of whether talcum powder can cause ovarian cancer. Plaintiffs' experts have also continued to examine the question. Contrary to the stilted and misleading picture painted in J&J's motion, these post-2020 developments *support* the PSC's causation experts.

One of the remarkable new developments since 2020 comes from cohort studies—a type of scientific study that tracks the life experience of tens of thousands of participants over a significant portion of their lives. Previously, J&J and its experts had argued to Judge Wolfson that cohort studies "provide more reliable results" than case-control studies—and argued that their supposed lack of support from the 2020 record was a reason to exclude Plaintiffs' experts' opinions. *In re J&J*, 509 F. Supp. 3d at 162.

Today, the "more reliable" data J&J said was unavailable has been collected, peer reviewed, and published. And this new data reaffirms and strengthens the case for a positive association between J&J's product and cancer.

For example, NIH scientists published a study of pooled cohort data (O'Brien 2020)[1] which found a positive association between talc and ovarian cancer, with a statistically significant positive association in women with intact

[1] Ex. 1, O'Brien et al., *Association of Powder Use in the Genital Area with Risk of Ovarian Cancer*, 323 JAMA 49 (2020).

reproductive tracts. In another study (O'Brien 2024)[2], these same NIH researchers published from a "large cohort of US women-Sisters Study" that similarly "found evidence supporting a positive association between ever genital talc use and incident ovarian cancer" which was "consistent with previous studies."[3] Moreover, a separate meta-analysis of cohort and case-control data (Woolen 2022)[4] found an almost 50% statistically significant increased risk of ovarian cancer for frequent talc users, including a 40% increase in women enrolled in a cohort study.

And that's not all. There have been significant developments since 2020 amongst national and international regulatory organizations. These, too, support Plaintiffs' experts. For example, in 2021 Health Canada (the Canadian version of the FDA) issued a final peer-reviewed comprehensive review of the epidemiologic and biological evidence which concluded that talcum powder causes ovarian cancer.[5] This past month, in July 2024, the World Health Organization's International Agency for Research on Cancer (IARC) conducted its own independent review and concluded that cosmetic talc *without* asbestos was a

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[2] Ex. 2, O'Brien et al., *Intimate Care Products and Incidence of Hormone-Related Cancers: A Quantitative Bias Analysis*, 42 J. Clin. Oncol. 2645 (Aug. 1, 2024).
[3] *Id*. at 13. See also Ex. 3, Harris et al., *Epidemiologic Methods to Advance Our Understanding of Ovarian Cancer Risk*, J Clin Oncol 00:1-3, 2 (May 15, 2024).
[4] Ex. 4, Woolen, et al., *Association between the Frequent Use of Perineal Talcum Powder Products and Ovarian Cancer: A Systematic review and Meta-Analysis*, 37 J. Gen. Intern. Med. 2526 (2022).
[5] Ex. 5, Health Canada, Screening Assessment Talc (April 2021) at p. iii, 36, 43, 45.

"probable" ovarian carcinogen and confirmed that talc *with* asbestos (which includes Johnson's Baby Powder and Shower to Shower) was an "established" ovarian carcinogen.[6] The NIH itself, in highlighting the work of its scientists, noted in 2024 that there was "compelling evidence that genital talc use is associated with an increased risk of ovarian cancer" particularly among frequent and long term users. [7] In 2023 and again in 2024, the Environmental Protection Agency (EPA) concluded that talc deposits have been shown to contain asbestos, and asbestos can cause ovarian cancer.[8] In 2021, an Interagency Working Group including representatives from the FDA, NIH, NIOSH, NEIHS, EPA, noted that asbestos in talc can cause cancer, and referred to the IARC assessment of talc and ovarian cancer.[9] In 2022, the Ovarian Cancer Association Consortium(OCAG), consisting of top researchers from leading cancer research hospitals around the world, has

[6] Ex. 6, Stayner et al., *Carcinogenicity of Talc and Acrylonitrile*, The Lancet (July 5, 2024); Ex. 7, IARC Monographs Evaluate the Carcinogenicity of Talc and Acrylonitrile: Questions and Answers (July 5, 2024).
[7] Ex. 8, NIH/NIEHS Environmental Factor, *Genital talc use may be linked to increase risk of ovarian cancer* (June 2024).
[8] 88 Fed. Reg. 47782, 47790 (July 25, 2023) (to be codified at 40 C.F.R. pt. 704); 89 Fed. Reg. 21970, 21970 & 21973 (2024).
[9] Ex. 9, *Preliminary Recommendations on Testing Methods for Asbestos in Talc and Consumer Products Containing Talc* (Jan. 6, 2020), at 1–2.

called the genital exposure to talcum powder a "well established ovarian cancer risk factor,"[10] a similar position taken by the Institute of Medicine (IOM).[11]

It is not Plaintiffs' experts who are "forging new trails in scientific thinking." (Mem. 7, 59 (citing *In re Acetaminophen I*).) Because J&J again urges this Court to reject Judge Wolfson's settled opinion, the party that wants to blaze a new trail is plainly *J&J*. This Court should limit the scope of J&J's challenge to the use of scientific evidence that is *truly* new and to the impact of any *truly* new law. And for the reasons below, the Court should deny this motion.

BACKGROUND

I. Chief Judge Wolfson's 2020 *Daubert* ruling.

The fundamental scientific question in this MDL is whether Defendants' talcum powder products, including Johnson's Baby Powder, can cause epithelial ovarian cancer. *In re Johnson & Johnson*, 509 F. Supp. 3d at 128. After a full

[10] Ex. 10, Phung M et al., *Effects of risk factors for ovarian cancer in women with and without endometriosis*, 118 Fertility and Sterility 960 (Nov. 2022). OCAC had previously published a pooled analysis of over 6,000 ovarian cancer cases and concluded that "genital powder use is a modifiable exposure associated with small-to-moderate increases in risk of most histologic subtypes of epithelial ovarian cancer." Ex. 11, Terry et al., *Genital Powder Use and Risk of Ovarian Cancer: A Pooled Analysis of 8,525 Cases and 9,859 Controls*, 6(8) Cancer Prev. Res. 811 (2013).

[11] Ex. 12, National Academies of Science, Engineering and Medicine, *Ovarian Cancers: Evolving Paradigms in Research and Care* at 110 (2016) ("The use of perineal talcum powder has been associated with a 20 to 30 percent increased risk of ovarian cancer . . . .").

evidentiary hearing, Chief Judge Wolfson concluded that "what remains clear from the general causation evidence relied on by the experts on both sides in this matter, is that there is relevant scientific evidence supporting each side's opinion." *Id.* at 187.

As this Court held in its April 30, 2024 Order permitting *Daubert* motions, either side could challenge Chief Judge Wolfson's 2020 ruling if that ruling "demonstrably fails" to adhere to amended Rule 702, or if there is new science that "is shown to directly contradict or challenge" that ruling. (ECF No. 32122 at 6.) As a predicate for considering those questions, Plaintiffs first examine the scientific record at the time of the 2020 *Daubert* order and then how Judge Wolfson reached her findings.

A. The state of the scientific record in 2020.

The question of whether talcum powder can cause ovarian cancer is one of longtime research. Henderson raised the issue in 1971 when it was shown that there were talc particles in 10 out of 13 ovarian tissue cancer samples.[12] Although the question persisted throughout the 1970's, the first epidemiologic study that was conducted was Cramer 1982, a case-control study that showed a dramatically increased risk of ovarian cancer with genital talcum powder usage (OR 1.92; 95%

[12] Ex. 13, Henderson, et al., *Talc and Carcinoma of the Ovary and Cervix*, 78 Brit. J. Obstetrics and Gyn. 266–72 (1971).

CI 1.27–2.89).[13] Over the years, the question has been examined through other observational studies, which, given the ethical considerations inherent in conducting clinical trials involving a suspected carcinogen, are the best way science has to measure any relationship.[14]

As of the date of the *Daubert* hearing in 2019, there were approximately 30 published case-control studies, five published studies done from three separate cohort studies, and eight pooled or meta-analyses. Each of these study designs have different strengths and different weaknesses. Generally, both sides attempted to grapple with all known studies. These studies are summarized below.[15] Appendices 1–3 to this brief summarizes all of these studies in greater detail.

Case-control studies. As of 2020, there were approximately 30 published case-control studies conducted over decades, involving dozens of authors, different study populations, and different countries.

In case-control studies, specific participants who are diagnosed with a specific type of cancer (the "cases") are compared with other specific participants who have not been diagnosed with cancer (the "controls"). Ideally, the cases are

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[13] Ex. 14, Cramer, et al., *Ovarian Cancer and Talc: A Case-Control Study*, 50 Cancer 372 (1982).
[14] Ex. 15, Rothman, et al., *Modern Epidemiology* (3d ed. 2009), at 25–26.
[15] For a more fulsome discussion of the science at the time, see the PSC's omnibus opposition brief to J&J's motion to exclude general causation opinions (ECF No. 9914) (May 31, 2019), and the PSC's "Post-*Daubert* Hearing Summation Brief" (ECF No. 10712) (Oct. 7, 2019).

similar to their controls on all variables other than the exposure under question. The investigators then analyze whether the cases are more likely than the controls to have a given exposure.

The benefits of case-control studies include the ability to enroll a large number of cases, being generally less expensive than cohort studies, and the ability to complete over shorter periods of time. Case-control studies focus on a single disease, so they are able to collect more detailed risk factor information for that disease than cohort studies. A major advantage of case-control studies is that they are a more efficient design for studying diseases that are less common or have a long latency period. Therefore, they are very often used for etiologic studies of cancer.

A potential disadvantage of case-control studies is that they collect exposure information for the cases after they have already been diagnosed with the disease, which raises concerns that cases may recall their exposures differently from controls—recall bias.[16]

Of the 30 case-control studies published between 1982-2016 involving *thousands* of diagnosed ovarian cancer cases, 28 of them showed a positive

[16] Federal Judicial Center, *Reference Manual on Scientific Evidence*, (3d ed. 2011) at 555–56.

association, with 17 of those being statistically significant.[17] Plaintiffs' experts consider that to be valuable information on causality.

The studies themselves, as well as Plaintiffs' experts, attempted to measure and eliminate the possible effect of recall bias and other confounders and errors in these studies. Most of the studies ultimately concluded that recall bias was not the explanation for the increased risk observed. For example:

- **Health Canada 2018.** "In studies where the exposure is simple (e.g., never versus ever use), recall bias is unlikely to be an important source of bias . . . ."[18]
- **Gates 2008.** "In addition, the exposure definition of genital talc use at least once a week may have decreased the influence of recall bias in this analysis, because habitual talc use is likely to be recalled more accurately than sporadic use."[19]
- **Mills 2004.** "Recall bias has also been implicated as a limitation in studies of talc and ovarian cancer. However, findings in a prospective study, the Nurses' Health Study, in which exposure data were collected prior to diagnosis and hence free of recall bias, were similar to the present study finding . . . . It has also been suggested that use of talc is habitual versus memorable and not likely to be subject to recall bias."[20]

[17] Appendix 1.
[18] Ex. 16, Health Canada, *Draft Screening Assessment, Talc* (Dec. 2018) at 28.
[19] Ex. 17, Gates, *Talc Use, Variants of the GSTM1, GSTT1, and NAT2 Genes, and Risk of Epithelial Ovarian Cancer*, Cancer Epidem. Biomarkers Prev. (Sept. 2008), at 9.
[20] Ex. 18, Mills, *Perineal Talc exposure and Epithelial Ovarian Cancer Risk in the Central Valley of California*, 112 Int'l J. Cancer 458–64, 464 (2004).

Cohort studies. In 2019, there were five published studies regarding talc and coming from three different cohorts—the Nurses' Health Study (NHS), the Women's Health Initiative (WHI), and the Sister Study.

In cohort studies, the exposures of a group (cohort) of people who are assumed to be healthy are assessed, and the group is followed over a long period of time. During the follow-up period, some members of the cohort may be diagnosed with cancer, while others will not. Comparisons are then made between these two groups.

Some of the disadvantages of cohort studies include the need for large numbers of participants and very long duration. To have sufficient statistical power to identify factors that increase cancer risk by 20 or 30 percent, cohorts may need hundreds of thousands of participants—particularly if the form of cancer was rare to begin with. Cohort studies also have to run for enough years to permit the cancer to appear—sufficient number of years to account for latency. Because the questions are asked ahead of time, responses can be difficult to interpret, leading to nondifferential misclassification bias, which has the potential of masking a true effect. Finally, if a cohort loses touch with study participants over all the years, information on them cannot be collected. One reason cohort study participants drop out is death from any cause.

None of the pre-2020 cohort studies was specifically designed to look at the talc/ovarian cancer link. As J&J pointed out, these studies followed more than 200,000 women. (Mem. at 10.) However, the absolute number of ovarian cancers in those cohorts was small—just over 2,000 cases.[21] For perspective, this was a fraction of the number of ovarian cancer cases in the case-control studies. (ECF No. 9914, PSC's 2019 Br. 122–26.)

In two of the three cohorts, WHI and NHS, the women were asked about "powder" generically, leading to the possibility that some of the women used cornstarch rather than talc—which would dilute the risk.[22] *Id*. at 125. One study cohort, Gonzales (2016),[23] only followed women for 6.6 years and asked only about recent talc use or use from ages 10–13, not lifetime talc powder use.[24]

Even with all these limitations, four of the five cohort publications arising from these studies prior to 2020 showed a positive association, albeit not a statistically significant one.[25]

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[21] Ex. 1, O'Brien 2020 at 52 & table 1.
[22] *Id*. at 57.
[23] Ex. 19, Gonzalez et al., *Douching, Talc Use, and Risk of Ovarian Cancer*, 27 J.u Epidemiology 797 (Nov. 2016).
[24] Ex. 2, O'Brien 2024 at 2 ("the initial questionnaire (used in Gonzalez) focused on two specific timeframes: age 10-13 years and the 12 months before enrollment").
[25] Appendix 2.

Meta-analyses and the pooled study. In 2020, there were eight available meta-analyses and one pooled study.[26] A meta-analysis is a statistical method of combining studies to increase the power to detect a rare disease.

The eight meta-analyses calculated summary relative risks that were very consistent across the publications, ranging from 1.22 to 1.35 (with all but one using a 95% confidence interval). These results showed that women who reported talc use were at increased risk of ovarian cancer. Four meta-analyses specifically evaluated genital talc exposure and risk of serous epithelial ovarian cancer—the most common type—revealing a significantly increased risk ranging from 1.24 to 1.38.[27]

Similarly, Terry 2013,[28] the pooled analysis of eight case-control studies and involving 8,536 ovarian cancer cases, reported an overall odds ratio of 1.24 (95% CI 1.15–1.33).

Thus, these "studies of studies" showed consistent and positive associations between talcum powder and ovarian cancer.

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[26] Appendix 3.
[27] Ex. 20, Penninkilampi & Eslick, *Perineal Talc Use and Ovarian Cancer: A Systematic Review and Meta-Analysis*, 29 J. Epidemiology 41 (2018); Ex. 21, Berge et al., *Genital use of talc and risk of ovarian cancer: a meta-analysis*, Eur. J. Cancer Prevention (2017); Ex. 22, Taher et al., *Critical review of the association between perineal use of talc powder and risk of ovarian cancer*, 90 Reproductive Toxicology 88 (2019); and Davis (see Appendix 3).
[28] Ex. 11.

Biological evidence. Plaintiffs' experts also reviewed the biological evidence that talcum powder applied to the genital area could migrate to the ovaries, cause an inflammatory response, and begin the process of carcinogenesis. (PSC's 2019 Brief, ECF No. 9914 at 165–78).

B. Judge Wolfson's 2019 *Daubert* hearing and 2020 *Daubert* ruling.

To address the question of general causation—and to assess and interpret the science described above—the parties named more than 35 experts in a variety of disciplines, including epidemiology, biology/oxidative stress, genetics, materials science, pharmacology, toxicology, pathology, and gynecologic oncology. *In re J&J* at 130. The parties filed over 1,000 pages of briefs and 500 exhibits.

Chief Judge Wolfson convened an eight-day evidentiary hearing in July 2019 to hear the parties' challenges to each side's experts. "Rather than calling every expert challenged by the motion," by agreement, "the parties selected certain experts as representatives of each field of science involved in [the] case." *In re J&J*, 509 F. Supp. 3d at 128. Each expert who appeared was subject to vigorous cross-examination on their methodologies and how they applied them to the evidence. The Court asked probing questions of each witness. Judge Wolfson's opinion was issued on April 27, 2020, and shows that she carefully examined each expert's report, testimony, and the evidence on which that expert relied.

With respect to the general causation witnesses, the parties and the Court focused on the familiar Bradford Hill causation factors, which each witness considered and applied to the scientific evidence.[29] With respect to the application of these factors, Judge Wolfson relied on the Federal Judicial Center's Reference Manual on Scientific Evidence. *Id.* at 160, n. 34 (discussing reliance on Manual).

And she examined "the reliability of each Bradford Hill factor" in turn, *id*. at 162, in a clear and separate section for each of the nine factors. The most hotly contested factors were strength of association; consistency of the epidemiologic studies; dose-response relationship; and biological plausibility.

One issue Judge Wolfson reviewed—in the context of the strength-of-association factor—was the role of the three cohort studies, which were not designed to address the risk of ovarian cancer. Although Plaintiffs' experts relied on and addressed all of the studies, J&J criticized them for not weighing the cohort studies as heavily as J&J's experts did. Judge Wolfson reviewed Plaintiffs' experts reasons for doing so, *id*. at 164–66, and found that "the general causation experts

[29] Ex. 23, Austin Bradford Hill, *The Environment and Disease: Association or Causation?*, 58 Proc. Royal Soc'y Med. 295 (1965). Those nine factors are: (1) temporal relationship; (2) strength of association; (3) dose-response relationship; (4) replication; (5) biological plausibility; (6) consideration of alternative explanations; (7) cessation of exposure; (8) specificity of the association; and (9) consistency with other knowledge. Green, et al., *Reference Guide on Epidemiology*, in *Reference Manual on Scientific Evidence* 549, 600. *See also In re Zoloft Prods. Liab. Litig.*, 858 F.3d 787, 795 (3d Cir. 2017) (Bradford Hill analysis is "generally reliable").

have demonstrated that their decisions to rely on the case-control studies . . . is supported by good grounds and does not constitute a 'rigid' dismissal of the cohort studies." *Id.* at 166. She went on to state that "this is not a situation where the experts purposefully ignored the cohort studies because they were inconsistent with their opinions." *Id*.

Another specific issue Judge Wolfson zeroed in on—this time in the consistency-of-the-evidence factor—was the role of statistical significance in interpreting data. Then, as now, J&J claimed that Plaintiffs' experts improperly considered certain data that showed an elevated ovarian cancer risk, but was not statistically significant. Judge Wolfson noted that the Third Circuit had "declined to adopt a bright-line rule" regarding statistical significance. *Id.* at 170 (quoting *In re Zoloft Prods. Liab. Litig.*, 858 F.3d 787, 793 (3d Cir. 2017)). She also quoted the *Zoloft* court to state that statistical significance is no "magic criterion." *Id.* After canvassing this law and what Plaintiffs' experts had opined on statistical significance, Judge Wolfson found that "the causation experts considered statistical significance with respect to both cohort and case-control studies, and did so in a reliable fashion." *Id*. at 170.

After reviewing all nine Bradford Hill factors, Judge Wolfson reached her conclusion: "the Court finds that the opinions of Plaintiffs' general causation

experts are admissible under Daubert," subject to certain limitations, because "[t]he experts reliably applied each factor of the Bradford Hill analysis." *Id*. at 187.

* * *

Judge Wolfson also cross-checked Plaintiffs' experts' opinions against available public health agencies' assessments of the talc/ovarian cancer risks. Finding no clear consensus on the topic—and finding that J&J "overstate[d] IARC's position on this issue"—Judge Wolfson found that Plaintiffs' experts did not disagree with any consensus by outside bodies. *Id*. at 185–86. Indeed, she found that the 2018 Health Canada draft assessment[30] supported Plaintiffs' position. *Id*. at 186. Accordingly, she declined to exclude Plaintiffs' experts on this basis. *Id*. As the Court will see later, Health Canada and other agencies have moved further toward Plaintiffs' position on the assessment of a risk.

* * *

Judge Wolfson's approach is entirely consistent with decisions *all* other courts have reached on *Daubert*-type admissibility questions.

Since the very first ovarian cancer case was tried in 2014, *every* court that has considered the general causation question—other than a New Jersey lower court that was later reversed—has agreed with Judge Wolfson that there is more

[30] Ex. 16.

than sufficient evidence that J&J's talcum powder can cause ovarian cancer and that the evidence should go to a jury. Those decisions include:

State	Citation	Attached as Exhibit
California	*Echeverria, et al. v. Johnson & Johnson, et al.,* No. BC628228, JCCP No. 4872 (Cal. Super. Ct. 2017) (Drs. Godleski, Plunkett, & Siemiatycki).	24
Florida	*Sugarman, et al. v. Johnson & Johnson, et al.*, No. 2019-CA-017627, Tr. 200:20–22; 210:1; 258:11–14 (Cir. Ct.–Miami-Dade County) (Feb. 9, 2024) (Drs. Rigler, Ness (epidemiologist), Chan (gynecologic oncologist), Plunkett).	25
Florida	*Matthey v. Johnson & Johnson, et al.*, No. 2018-CA-004809-NC (Cir. Ct.–Sarasota County) (Mar. 30, 2024) (Drs. Rigler, Plunkett, Ness (Epidemiologist)).	26
Georgia	*Brower*, *et al.* v *Johnson & Johnson, et al.*, No. 16-EV-5534-E (Ga. Super. Ct.–Fulton County) (Mar. 26, 2019) (Drs. Godleski, Plunkett, Barter (gynecologic oncologist)).	27
Illinois	*Cadagin, et al. v. Johnson & Johnson, et al.,* Tr. 34:4-10 (Dr. Godleski); 53:20-54:10 (Dr. Plunkett); 79:19-80:7 (Dr. Rigler) (Apr. 20, 2021).	28
Missouri	The following decisions are illustrative. Plaintiffs' experts have testified in all nine trials in the City of St. Louis, Missouri. ▪ *Daniels, et al. v. Johnson & Johnson, et al.,* No. 1422-CC09326-01 (City of St. Louis, MO) (Feb. 6, 2017) (Drs. Plunkett, Godleski, and Siemiatycki).	29, 30, 31

State	Citation	Attached as Exhibit
	▪ *Hogans, et al. v. Johnson & Johnson, et al.*, No. 1422-CC09012-01 (City of St. Louis) (Jan. 15, 2016) (Drs. Ness and Godleski).	
New Jersey	*Carl v. Johnson & Johnson*, 464 N.J. Super. 446 (App. Div. 2020), *cert. denied*, 245 N.J. 144 (2021).	—
Pennsylvania	*Kleiner, et al. v. Johnson & Johnson, et al.,* No. 2505, Phila.–Com. Plea (May 22, 2020) (Drs. Godleski, Plunkett, Smith-Bindman, Saed, and Wolf).	32
South Dakota (federal court)	*Deane Berg v. Johnson & Johnson, et al.*, 940 F. Supp. 2d 983 (D.S.D. 2013)	—

The decisions of the New Jersey state courts are particularly instructive. The Law Division judge held an evidentiary hearing on the general causation question, and in 2016, found that there was no reliable evidence that talc could cause ovarian cancer. *Carl v. Johnson & Johnson*, No. ATL-L-6456-14, 2016 WL 4580145 (N.J. Super Ct. Law Div. Sept. 2, 2016). J&J trumpeted the Law Division's opinion to Judge Wolfson, but she declined to follow it, noting that the federal MDL record involved more studies and more recent studies than the Law Division had before it. *Id.* at 163 n. 38.

Ultimately, plaintiffs in New Jersey were vindicated, because the Appellate Division reversed the decision excluding their experts. *Carl v. Johnson & Johnson*, 464 N.J. Super. 446 (App. Div. 2020), *cert. denied*, 245 N.J. 144 (2021). The

Appellate Division examined the same Bradford Hill criteria as Judge Wolfson and concluded that "plaintiffs' experts provided admissible opinions meeting the [federal Reference] *Manual* and *Hill* protocols." 464 N.J. Super at 496. Further, the court held that "cohort, case control and pooled or meta-analyses" offered "considerably more than minimal support for the association of talc and ovarian cancer, whether they are considered together or just by kind of study." *Id.* at 499. And it found that the Law Division erred by "select[ing] defendants' scientific methodologies over plaintiffs', a process well beyond the gatekeeping function." *Id.* at 504.

If this Court were to disturb Judge Wolfson's findings, it would stand alone—even among states where the *Daubert* standard is observed—in rejecting the admissibility of Plaintiffs' general causation opinions.

II. The scientific and regulatory record after 2020.

There have been at least three scientific major developments since 2020 that further support and affirm the correctness of Judge Wolfson's opinion. First, it is now generally accepted that cosmetic talcum powders—including Johnson's Baby Powder—contained asbestos. Second, numerous new publications, primarily from cohort data, support a statistically significant association between talcum powder and ovarian cancer, particularly in women with an unobstructed pathway between the genital area and the ovaries. Third, United States and international scientific

bodies have concluded that talcum powder is, in fact, associated with and causes ovarian cancer.

A. It is now generally accepted that talcum powders contain asbestos.

At the time of Judge Wolfson's *Daubert* order in 2020, the composition of Johnson's talcum powders was in hot dispute, with the plaintiffs contending that they contained asbestos, and J&J insisting that its talc was mined from "pure" sources and that tests have always shown its talc to be "asbestos free." The resolution of whether cosmetic powders contain asbestos is critical since the presence of asbestos, a known carcinogen, would provide additional evidence in support of Plaintiffs' contention that talcum powder could cause ovarian cancer.[31]

Since 2020, the regulatory and scientific community has accepted that cosmetic talc products have, in fact, contained asbestos. Critically, the FDA found asbestos in Johnson's Baby Powder in October 2019, *after* the July 2019 *Daubert* Hearings.[32] Following that finding, the FDA, the NIH, the EPA and other

[31] J&J's own consultants and experts agreed. While asserting that talc was asbestos free, its experts agreed that the presence of asbestos would support a causal inference: "Clearly, [talcum powder] products could possibly present a carcinogenic risk secondary to the asbestos contamination. It should be pointed out that this in no way implicates talc as a toxin[,] as the problematic constituent of such products was the asbestos fibers, not talc." Ex. 33, Huncharek & Muscat, Perineal talc use and ovarian cancer *risk: a case study of scientific standards in environmental epidemiology*, 20 Eur. J. Cancer Prevention 501, 505 (2011).

[32] Ex. 34, FDA, *Johnson's Baby Powder voluntarily recalled after testing positive for asbestos* (Oct. 18, 2019). While the FDA testing was available before Judge Wolfson rendered her opinion in 2020, it was not available at the time of the

government agencies formed an Interagency Working Group on Asbestos and Consumer Products Containing Talc (IWACP). The IWACP acknowledged "long-recognized shortcomings in . . . specificity and sensitivity" of the testing used by the talc industry to screen cosmetic talc for asbestos and recommended more stringent screening of talc.[33] Since that time, the EPA has reiterated that talc mined for use in consumer products like talc powder may contain asbestos, a proposition that J&J has steadfastly denied.[34]

More recently in 2024, IARC re-reviewed whether talc *without* asbestos could cause ovarian cancer. Although it concluded that talc (platy and fibrous) powder alone, without asbestos, "probably" causes ovarian cancer, it concluded that these powders *with asbestos* definitively causes ovarian cancer. In so finding, IARC emphasized that asbestos "contamination with talc products has been documented and [] industry standards used to assess talc in cosmetic and

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Daubert hearings in July 2019. The Court was made aware of the FDA testing on Oct. 29, 2019 (ECF No. 10938).

[33] Ex. 9 at 2. See also Ex. 35, Appendices to White Paper: IWGACP Scientific Opinion on Testing Methods for Asbestos in Cosmetic Products Containing Talc (Dec. 2021), App'x F, at 55.

[34] 86 Fed. Reg. 74088 (Dec. 19, 2021) ("talc has been implicated as a potential source of asbestos exposure"); 88 Fed. Reg. 47782, 47784 (Jul. 25, 2023) ("asbestos is being mined or milled . . . as an impurity" in talc); 89 Fed. Reg. 21970, 21970, 21973 (Mar. 28, 2024) ("Additionally, some talc deposits and articles containing talc have been shown to contain asbestos.").

pharmaceutical products have often not been sufficiently sensitive to rule out contamination with asbestos."[35]

Since 2020, the scientific literature has also acknowledged that cosmetic talc products contain asbestos. For example, one article in 2021 by O'Brien and Wentzensen noted that:

> Talc can be contaminated with a variety of other minerals. **Most important are contaminations with asbestos** or quartz, both class 1 carcinogens according to IARC (which means that there is enough evidence to conclude that these substances can cause cancer in humans), which frequently co-occur naturally with talc. . . . **While talc products since the 1980s have been considered asbestos-free, recent reports have suggested that low-level contamination of talc with asbestos fibers may have persisted in some cosmetic products.**[36]

The bellwether plaintiffs *daily* applied Johnson's Baby Powder and/or Shower to Shower to their genital area for decades—the shortest period being 20 years, the longest being 55 years, and the average being just over 42 years.[37] The

[35] Ex. 7, IARC, *Questions and Answers*, at 4. *See also* Ex. 6, Stayner, at 1 ("asbestos has been reported to be present in some talc ores and talc products as a contaminant. Industry standards used to assess talc-based cosmetic . . . products have often been insufficiently sensitive to rule out asbestos contamination.").
[36] Ex. 36, Wentzensen & O'Brien, Talc, body powder, and ovarian cancer: A summary of the epidemiologic evidence, 163 Gynecol. Oncol. 199 (2021), at 200 (emphasis added).
[37] Ex. 37, William E. Longo, Jr., Expert Report, MDL Johnson's Baby Powder Application and Exposure Container Calculations for Six Ovarian Cancer Victims Bellwether Cases.

number of lifetime applications range from approximately 7,000 to 20,000. Over the course of these decades, bellwether Plaintiffs used between 221 and 568 containers of Johnson's Baby Powder and Shower to Shower.[38]

For each Plaintiff, the majority of the usage was during the time period when J&J sourced talc from Vermont. Drs. Longo and Rigler found that more than 75% of samples manufactured during that contained asbestos.[39] For the time period after 2003 when talc was sourced from China, Drs. Longo and Rigler identified asbestos in more than 80% of the samples.[40]

B. There are important new cohort studies that support a causal association between talcum powder and ovarian cancer.

As noted above, at the time of the prior *Daubert* ruling, there was data on cosmetic powders and ovarian cancer from three prospective cohort studies, the WHI, the NHS and the Sister Study. While four of the five publications arising from these cohorts showed a positive association between genital talc use and ovarian cancer, J&J pointed out that none showed a statistically significant positive association for epithelial ovarian cancer.[41] According to J&J, the failure of the cohorts to reach statistical significance was dispositive of the causation question. *In re J&J*, 509 F. Supp. 3d at 169 ("Defendants argue that because no cohort study

[38] *Id*.
[39] *Id*.
[40] *Id*.
[41] Appendix 2.

concluded there was a statistically significant association between talc use and ovarian cancer, the two types of studies cannot be consistent.").

As Plaintiffs' experts explained at the time, however, these three individual cohort studies had significant limitations because, among other things, they: were underpowered to detect a result, collected limited and incomplete data about talcum powder use, did not run long enough to account for the latency of cancer, and were not specifically designed to study the talc and ovarian cancer question. *Id.* at 165–66. Moreover, Plaintiffs' experts testified that there were biases in these cohort studies that would attenuate or mask a true association. Under those circumstances, Judge Wolfson agreed that Plaintiffs' experts did not rigidly "dismiss[] the cohort studies outright." *Id*. at 171.

Since 2020, there have been several studies which address the shortcomings of the cohort data available to Judge Wolfson. These studies have statistically significant results that support a positive association.

1. O'Brien 2020

In O'Brien 2020, NIH scientists noted what Plaintiffs' experts had explained to Judge Wolfson in 2019—that the individual cohorts from 2020 were simply not powered to detect a "modest" association:

> To date, 3 large cohort studies have assessed the association between use of powder in the genital area and ovarian cancer risk, with inconsistent results. However, ovarian cancer is a rare disease (1.3% lifetime risk in the

> United States), and individual cohort studies are not sufficiently powered to detect modest associations, particularly if restricted to susceptible subgroups, such as women with patent reproductive tracts (ie, having an intact uterus and no tubal ligation).[42]

To increase the "power," to detect a risk, the authors of O'Brien 2020 pooled the data from the three cohort studies. Even though the total number of enrollees was large (over 200,000 participants), the total number of ovarian cancer cases remained modest (2,168 cases).[43] Nevertheless, the O'Brien 2020 pooled study sought to determine the overall risk to all women—including women with both open and closed reproductive tracts. The particular interest was on women who had open, intact reproductive tracts ("patent tubes").[44] When the analysis was done, the researchers found an increased overall risk of 1.08 (CI 0.99–1.17)—an 8% increased risk. Notably, they also found a statistically significant increased risk of 1.13 (CI 1.01–1.26) in the susceptible subgroup, women with open reproductive tracts.

The O'Brien authors agree with Plaintiffs' experts that their pooled cohort study—both the overall result and the patent tube result—support an association.

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[42] Ex. 1, O'Brien 2020 at 50.
[43] *Id.* at 49. The authors acknowledged that even their pooled study might not be big enough.
[44] *Id.* at 51. The reason for the interest in the "patent tube" subgroup was because "patency is required for there to be a direct pathway between the application area and the ovaries."

For example, in response to a *Letter to the Editor* by Harlow and Rothman, the NIH authors responded by clarifying that their overall findings were positive and, in fact, likely underestimated the true risk of association:

> **If cohort studies (pooled HR, 1.08) are likely biased toward the null and case-control studies (meta-analysis OR, 1.35) are likely biased away from the null, the true association may lie somewhere in the middle.**
>
> We completely agree with Dr Harlow and colleagues that our results, particularly the analyses limited to women with intact reproductive tracts, should not be discounted because of lack of statistical significance. . . . [W]**e never equated the lack of statistical significance to evidence of no association**.[45]

With respect to the findings in women with patent reproductive tracts, the NIH authors again explained that these were important findings that *support* an association between talc and ovarian cancer. They wrote, "we . . . agree that the positive association among women with patent reproductive tracts (HR, 1.13; 95%CI, 1.01-1.26) is consistent with the hypothesis that there is an association between genital powder use and ovarian cancer."[46]

In numerous articles published since 2020, O'Brien and colleagues have emphasized that the results of their 2020 pooled study showed a positive

[45] Ex. 38, O'Brien et al., Letters to the Editor, 323 JAMA 2095, 2097 (May 26, 2020).
[46] *Id*.

association that was likely understated, particularly among women with intact genital tracts. They have written:

- "The epidemiologic literature *supports* a possible positive association between genital talc use and ovarian cancer."[47]
- "[T]he results of the prospective [cohort] studies [citing O'Brien 2020] ***support*** the hypothesis that the ***positive*** association between genital powder use and ovarian cancer may be limited to women with patent reproductive tracts."[48]
- "The HR from a pooled analysis of prospective cohort studies also indicated a positive, albeit small association (HR 1.08), and as previously noted, this effect estimate is likely biased toward the null because of nondifferential misclassification of exposure."[49]
- "[Since 2006] more consistent positive associations have been reported in pooled cohort studies and case control studies . "[50]

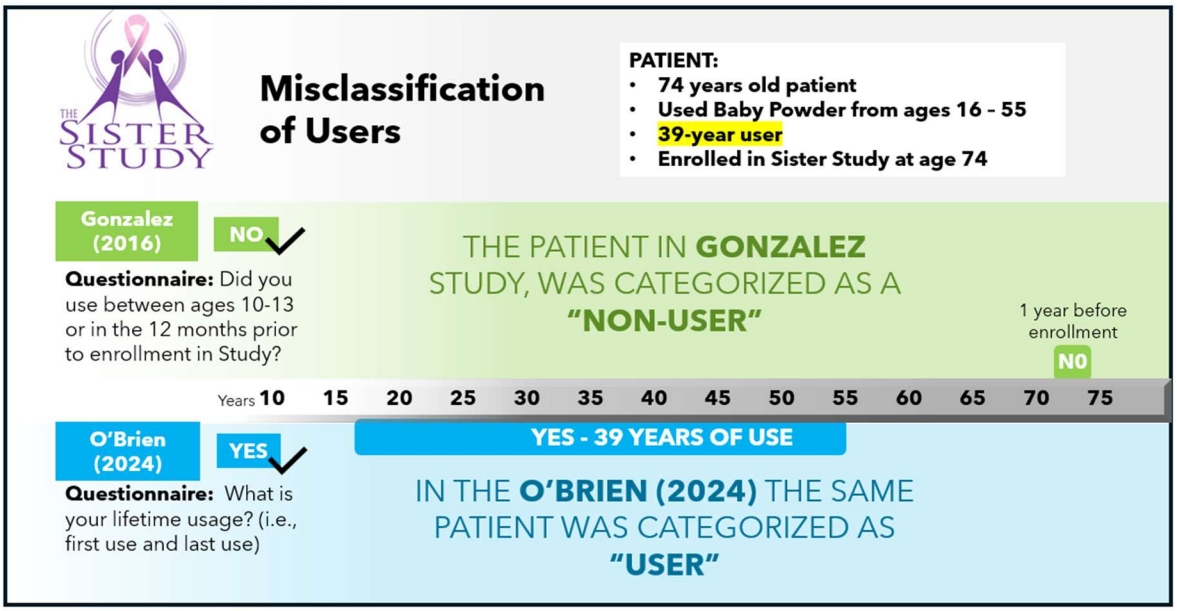
2. O'Brien 2024

Following O'Brien 2020, NIH researchers returned to the Sister Study cohort that supplied the data for their earlier publication, Gonzales 2016.[51] In Gonzalez 2016, the authors had used a limited study questionnaire that did not ask about long-term talc use or lifetime talc use. The enrollment questionnaire used in

[47] Ex. 39, O'Brien, et al., The association between douching, genital talc use, and the risk of prevalent and incident cervical cancer, 11 Nature 14836, 2 (2021) (emphasis added).
[48] Ex. 36, Wentzensen & O'Brien, at 8.
[49] Ex. 2, O'Brien 2024 at 13.
[50] Ex. 6, Stayner at 2.
[51] Ex. 19, Gonzales 2016.

Gonzales 2016 only asked whether the woman used powder between ages 10–13, or, a year before study enrollment.

That was a significant limitation of the data: since the enrollees were between 37 and 74 years old, the questionnaire used could miss *decades* of talc use. (E.g., a 74-year-old enrollee would have been asked about ages 10–13, age 73, but not ages 14–72.) To illustrate the gaps left by the questionnaire used to measure talc use in the Gonzales study, see this graphic prepared by counsel:



To compound the problem, the O'Brien authors conducted a study in 2023 and learned that the most likely years women use talcum powder are the 20's and 30's. This was, of course, the exact timeframe that the original study questionnaire used in Gonzalez 2016 missed. As the authors noted, it was possible for women to

use talcum powder for decades but be identified as "nonusers" because they weren't asked about use during the decades they were most likely to use it.[52]

To address these deficiencies and others, the Sister Study investigators conducted O'Brien 2024. In that study, they used a follow-up questionnaire which *did* ask about lifetime use, so they were able to capture the missing years not reviewed by Gonzales 2016. In addition, they had almost double the number of ovarian cancer cases because the follow up period had doubled from 6.6 years in Gonzales to 13 years in O'Brien 2024.

After accounting for women who were lost to the cohort before they could answer the follow-up questions about lifetime use (for example, those who had already died), the authors found a statistically-significant increased risk of 1.82 (CI 1.36–2.43), or 82% increase risk, which became even more pronounced with long term talc use.

The NIH authors further noted that the study was consistent with the positive results found in their pooled study, O'Brien 2020, and supported a positive association between genital talc use and ovarian cancer, even when the potential for recall bias was factored in.[53]

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[52] *Id*. at 4.

[53] For further discussion of O'Brien 2024, see Ex. 40, Rebuttal Expert Report of Elizabeth A. Stuart, Ph.D (July 21, 2024).

Recognizing the importance of the study findings, the NIH issued a press release that notes the evidence "supports a potential association between long-term and frequent genital talc use and ovarian cancer."[54]

3. Woolen 2022

Woolen 2022[55] was designed to estimate whether there is an association between frequent use of genital talc and ovarian cancer. Woolen looked at both case-control and cohort study data that reported talc use of two or more times a week. Among other things, the Woolen authors looked at daily use data from the Nurses' Health Cohort Study, to determine whether frequent exposure was related to ovarian cancer. The authors found "frequent use of perineal talcum powder was associated with an increased risk of ovarian cancer, with a pooled adjusted odds ratio of 1.47 (CI 1.31–1.65), or a 47% increased risk." Looking solely at the Nurse's Health Study cohort data, the odds ratio was 1.40 (CI 1.31–1.65).

4. Chang 2024

Chang 2024[56] was also an NIH study involving the Sister Study cohort. Its goal was to look a variety of personal care products, including talc powder, and see whether there was a "joint effect of multiple product exposure." While the body of

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[54] Ex. 8.
[55] Ex. 4.
[56] Ex. 41, Chang et al., *Use of personal care product mixtures and incident hormone-sensitive cancers in the Sister Study: A U.S.-wide prospective cohort*, Environment Int'l 183 (2024).

the paper did not discuss the risk ratio, Supplemental Table S5 provided a HR of 1.06 for a "one unit increase in talc frequency, i.e., in a woman who used it 1X a week." As the article pointed out, however, "Although the observed effects of a one-frequency level increase were modest in magnitude, the impact would be more substantial when comparing the most frequent users." Id. at 14. Thus, for a 5-day/week frequency user, the risk would be 1.26 compared with nonusers.[57]

5. Davis 2021

Davis 2021[58] was large case-control study involving over 3,000 cases which included data from a cohort study (WHI) and which examined whether the ovarian cancer risk talc was different between African American and white women. There was no concern of recall bias in the cohort data included in the study. Further, there was limited concern for recall bias in the retrospective cases because the author's only used data collected before 2014 (when the first ovarian cancer lawsuit was publicized).[59] The study concluded that there was a similar 30–35% increased risk seen in both African-American and white women.

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[57] Ex. 42, Deposition of Anne McTiernan, PhD, 22–24, 171, 173–77, 184; Ex. 43, Ex. D17 to McTiernan Dep.
[58] Ex. 25, Davis, *Genital powder use and risk of epithelial ovarian cancer in the Ovarian Cancer in Women of African Ancestry Consortium*, 30(9) Cancer Epidemiol. Biomarkers Prev. 1660 (2021).
[59] *Id*. at 9.

C. Regulatory authorities and professional organizations have now found a causal association between talcum powders—with and without asbestos—and ovarian cancer.

Since 2020, regulatory authorities, international scientific organizations have weighed in and *have* concluded that cosmetic talc powder—with or without asbestos—can cause ovarian cancer. These include Health Canada (2021), IARC (2024), EPA (2023 & 2024), and the Ovarian Cancer Association Consortium (2022):

- **Health Canada.** In her opinion, Judge Wolfson noted the Bradford Hill analysis contained in the Draft Health Assessment performed by Health Canada, the Canadian regulatory equivalent to the FDA.

  In 2021, Health Canada issued its Final Health Assessment.[60] That final assessment considered the MDL expert reports of both Plaintiffs and Defendants. During this period, J&J engaged with Health Canada and made sure it received the MDL reports of Defendants' general causation experts, including Drs. Merlo and Diette.[61]

  Health Canada performed its own full Bradford Hill analysis. It noted that the Bradford Hill factors are "considerations continue to be employed today, with some modified interpretations" which "under[went] external peer review."[62]

  After an exhaustive analysis of the epidemiologic and biologic evidence (including O'Brien 2020), Health Canada concluded that:

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[60] Ex. 5, Health Canada 2021.
[61] In footnote 160 of its brief, J&J makes the unsubstantiated suggest that Health Canada was "potentially influenced" by plaintiff and their experts." To the contrary, it was J&J which met with and sought to influence Health Canada to "change its mind," submitting a 5,000-page submission which included a misleading assertion that their product never contained asbestos.
[62] Ex. 5 at 2.

> With regards to perineal exposure, analyses of the available human studies in the peer reviewed literature indicate a consistent and statistically significant positive association between perineal exposure to talc and ovarian cancer. *The available data are indicative of a causal effect*. Given that there is potential for perineal exposure to talc from the use of certain self-care products (e.g., body powder, baby powder, diaper and rash creams, genital antiperspirants and deodorants, body wipes, bath bombs, bubble bath), a potential concern for human health has been identified.[63]

Health Canada ultimately held that "the available data are indicative of a causal relationship,"[64] and banned talcum powder products from the country.

- **The International Agency for Research on Cancer (IARC).** In her 2020 opinion, Judge Wolfson noted that IARC had classified Talc as a "possible" ovarian carcinogen in 2006.[65] That changed in 2024 when IARC re-reviewed talc on a priority basis. Looking at the totality of the scientific evidence as of 2024 (including O'Brien 2020), IARC upgraded talc without asbestos from "possibly carcinogenic" (Group 2B) to "***probably* carcinogenic**" (Group 2A) with respect to ovarian cancer (emphasis added).[66] Important to the issues in this case, IARC reaffirmed its 2012 classification that talc ***with asbestos*** is, without question, an ovarian carcinogen (Group 1). In a particularly misleading assertion that is emblematic of the way in which J&J cherry-picks partial quotes and takes them out of context, J&J's brief says (and then repeats) that Dr. O'Brien (who was on the IARC panel) disavows that conclusion because she said the human evidence was "not strong enough to say that talc causes ovarian cancer."[67] That is untrue. Dr. O'Brien's full quote makes clear that talc (the mineral) probably causes cancer but definitely does so

[63] *Id*. at iii.
[64] *Id*. at 36.
[65] 509 F. Supp. 3d at 185
[66] Ex. 6, Stayner.
[67] Mem. at 6 n.7, 25 n.67.

when it is contaminated with asbestos (like Johnson's Baby Powder is). Dr. O'Brien's full quote is:

> I worked with a panel of other scientists to evaluate the studies used in the IARC report on talc. *The studies provided evidence that talc is probably carcinogenic to humans.* The evidence was strongest in human cell and animal studies, but there were also many epidemiological studies that consistently showed an increased incidence of ovarian cancer among women who reported using talc powder in the genital region. Self-reporting can sometimes be unreliable, *and there's another confounder – asbestos. Talc powder may contain traces of asbestos, which is also a carcinogen.* So, the human study evidence was not strong enough to say that talc causes ovarian cancer.
>
> Industry standards for testing for asbestos in talc-based consumer products are not sufficient to rule out asbestos contamination, *and therefore we could not determine whether the link between body powders and ovarian cancer is due to talc or asbestos*. Women should consider the possible health effects of both talc and asbestos when they make decisions about using body powder and other talc-based personal care products.[68]

- **The Environmental Protection Agency.** In 2023, the EPA issued a final rule under the Toxic Substances Control Act (TSCA). In this final rule, the EPA concluded as follows: (1) asbestos may occur as an impurity in talc; (2) talc deposits can contain asbestos as an impurity; and (3) asbestos can cause ovarian cancer. [69] A year later, in 2024, the EPA again addressed the issue with a final rule related to the use of chrysotile asbestos. In this rule, the EPA stated as follows: (1) talc deposits and articles that contain talc have been shown to contain asbestos; and (2) chrysotile asbestos can cause ovarian cancer.[70]

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[68] *See* Ex. 44, Fidalgo, *Talc is classified as "probably carcinogenic to humans" by the IARC*, Science Media Center Spain (May 7, 2024).
[69] 88 Fed. Reg. 47782, 47790 (July 25, 2023) (to be codified at 40 C.F.R. pt. 704).
[70] 89 Fed. Reg. 21970, 21970 & 21973.

- **National Institutes of Health.** In its feature of O'Brien 2024, the NIH noted that there is now "compelling evidence" that genital talc use is associated with an increased risk of ovarian cancer, particularly among "long term users."[71]

- **The Ovarian Cancer Association Consortium (ACAC).** OCAC is a continuum of leading cancer research hospitals. In 2022, in an article by Phung, the OCAC consortium, listed "talcum powder (i.e. talc) use" as a well-established ovarian cancer risk factor." [72]

By contrast, J&J's preferred regulatory authorities and professional organizations have *not* performed a systematic review of the totality of the evidence.

In the very first sentence of its brief, J&J posits that "medical organizations and US Governmental Agencies have consistently agreed that the scientific evidence does not support the conclusion that talc is a cause of ovarian cancer. At best, that is a distortion of the evidence. At worst, it's a knowing misstatement.

First, and as set forth above, the EPA and NIH *have* concluded that Talcum powder causes and is significantly associated with ovarian cancer (not to mention Health Canada and IARC). Moreover, OCAC has determined that talcum powder is a well-established risk factor.

Second, even the organizations that J&J relies on have disavowed reaching that conclusion that talc is safe. For example:

[71] Ex. 8, NIH/NIEHS Environmental Factor.
[72] Ex. 10, Phung 2022.

- **Clinical Guidance for the American College of Obstetrician and Gynecologists (ACOG).** Plaintiffs attach the affidavit of Nancy O'Reilly, MHS, PMP, Senior Director, Clinical Guidance for the ACOG, an organization that J&J relied on to support its position.[73] As the O'Reilly affidavit makes clear, ACOG "did ***not*** reach [ ] a clinical conclusion was to whether there was a causative link between the use if talcum powder and ovarian cancer," "has *not* performed a systematic review on the use of talcum powder and ovarian cancer," and 'has *not* issued any clinical guidance of conclusions regarding potential risk or the safety of genital talc application and talcum powder."[74]

- **NCI PDQ:** Similarly, throughout its brief J&J relies on the "NCI PDQ" as a statement of the "National Cancer Institute (NCI)."[75] Preliminarily, the PDQ is not a systematic review and does not purport to review all the evidence and, in particular, has not been updated to include a discussion of O'Brien 2024 or the IARC reclassification of talc as a "probable carcinogen." More importantly, the PDQ specifically states that it "does **not** represent a policy statement of NCI or NIH."[76]

- **FDA.** Finally, J&J relies on 2014 letter from FDA responding to a "citizen's petition" to require a cancer warning. In that 10-year-old letter, which J&J already argued to Judge Wolfson, Dr. Musser states only that it had no "conclusive' evidence at that time. Importantly, however, this letter states that evidence of talc migrating to the ovaries is "indisputable" and that the "best evidence for an association relationship between genital talc exposure and ovarian cancer comes from epidemiologic data which show q statistically significant but modest increased risk of epithelial ovarian cancer…" [77]

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[73] Mem. 1, n.1.
[74] Ex. 45, Affidavit of Nancy O'Reilly, MHS, PMP (Aug. 14, 2024).
[75] Mem. 24, 20, 47, 64.
[76] Nat'l Cancer Inst., *Ovarian, Fallopian Tube, and Primary Peritoneal Cancers Prevention (PDQ®)*, available at https://www.cancer.gov/types/ovarian/hp/ovarian-prevention-pdq.
[77] Ex. 46, Letter from Steven Musser, MD (Apr. 1, 2014) at 5.

To buttress its contention that post-2020 studies support its contention, J&J relies on industry-funded articles which have no additional data but have a lot of company "spin." *E.g.*, Mem. 47–48, n.121 & 122 (citing Lynch, *Systematic Review of the Association Between Talc and Female Reproductive Tract Cancers*, 5 Frontiers in Toxicology 1 (2023)); Mem. 12 (citing Goodman, *Quantitative Recall Bias Analysis of the Talc and Ovarian Cancer Association,* 7 Glob. Epidemiol. 1 (2024), p. 12, 19, n 23, 41). Lynch 2023 was authored by consultants to corporate law firms, three of who are expert witnesses for talc defendants who do not appear in this MDL, and their paper is simply a review of previously published data, not original research. Similarly, Goodman 2024 was authored by employees of a consulting firm which has lobbied governmental agencies like Health Canada on behalf of talc companies and was provided in the context of litigation. Funding for Goodman 2024 was provided by the mining and cosmetic industry.

III. Plaintiffs' expert witnesses, their opinions, and their methodologies.

The following experts were designated by the PSC to testify that J&J's products are capable of causing epithelial ovarian cancer. Unlike J&J's experts, most of plaintiffs' experts have published in the peer-reviewed literature and/or

engaged with the scientific and/or regulatory community on the matters upon which they are prepared to testify.[78]

A. Anne McTiernan, MD, PhD

Dr. McTiernan is a Full Research Professor at the Fred Hutchinson Cancer Center in Seattle, Washington, Division of Public Health Sciences Program in Epidemiology. She is also a Full Research Professor at the University of Washington, School of Public Health's Department of Epidemiology and the University of Washington School of Medicine, as well as a cancer prevention researcher.[79]

Dr. McTiernan has spent the past 30 years in epidemiologic research, working primarily in the areas of cancer and women's public health. During this time, she has published over 450 manuscripts in peer-reviewed medical and scientific journals including publications in the area of ovarian cancer and gynecologic cancers in general.[80] Significant to her opinions in this case is the fact that she served as Project Director for clinical work from the inception of the 2014 Women's Health Initiative ("WHI") cohort study, a study which has published

[78] For example, J&J's two main causation witnesses, Gregory Diette, M.D. and Christian Merlo, PhD, are pulmonologists who have not published on talc, ovarian cancer, or even any other gynecologic cancer.
[79] Ex. 47, Third Amended Expert Report of Anne McTiernan, MD, PhD (May 28, 2024) at 1 and Ex. A.
[80] *Id.* at 3–5.

papers on talc and ovarian cancer.[81] Dr. McTiernan has lectured on the topic of talc and ovarian cancer and presented testimony on this subject to the United States House of Representatives Subcommittee on Economic and Consumer Policy in 2019.[82]

Dr. McTiernan's methodology consisted of collecting and thoroughly reviewing and analyzing available and relevant published epidemiological studies, including case-control and cohort studies, systematic reviews, meta-analyses, and pooled analyses to assess whether perineal use of Talcum Powder Products can cause ovarian cancer.[83] Her research included and considered studies that both support and do not support her opinions.[84] Given the presence of asbestos found in cosmetic and personal use talc products, she also reviewed the literature on the epidemiology of asbestos and risk of ovarian cancer including examining the biologically plausible mechanisms to explain the carcinogenic effects of talcum powder products.[85] In her review of the observational studies, she specifically examined the strengths and weaknesses of each study, evaluating the potential biases inherent in each study and the possible effects of confounding on the

[81] *Id.* at 5–6.
[82] Ex. 48, Report of Anne McTiernan to the House of Representatives Subcommittee on Economic and Consumer Policy (Mar. 12, 2019).
[83] Ex. 47, McTiernan Rep. at 8, 33–34.
[84] *Id.* at 33.
[85] *Id*. at 10, 84–88.

reported results.[86] In addition, she collected and considered biological, pathologic and mechanistic evidence, including evidence on the transport of talcum powder to the ovaries, the effect of talcum powder on cells, and the presence of carcinogens (including asbestos) in the product. Having collected the observational, biologic and pathological evidence, she analyzed it according to the Bradford Hill aspects of causation and weighed the quality of evidence supporting or detracting from each piece of evidence. Having done so, Dr. McTiernan expressed her opinions as an epidemiologist and physician to a reasonable degree of medical and scientific certainty that Talcum Powder Products, including Johnson & Johnson Baby Powder and Shower to Shower, in the genital/perineal area can cause ovarian cancer.[87] She bases this opinion "on the statistically significant elevated risk estimate (22–31%) seen when the epidemiologic data are combined, the pathological evidence, the consistency of results across geographic areas and in different race/ethnic groups, the evidence of a positive dose response effect, and the plausible biological mechanisms.[88]

[86] *Id*. at 8–11, 33–34.
[87] *Id*. at 10.
[88] *Id*. at 10–11.

Importantly, the methodology employed by Dr. McTiernan for purposes of her general causation opinions was found to be reliable and admissible by this Court following the extensive Daubert process which concluded in 2020.[89]

In Dr. McTiernan's most recent amended report of May 2024, she reviewed and considered newly published literature relevant to her opinions since 2020.[90] This review of the epidemiologic data included newly published original research, meta-analyses and studies by NIH/NCI researchers. Her review included the 2024 O'Brien study, an extensive analysis conducted using information collected from women in the Sisters Study cohort, which incorporated adjustments for potential biases and missing data. It was Dr. McTiernan's opinion that these new data and analyses added further strength to aspects of her Bradford Hill causal analysis, including strength of association, consistency of the association, specificity of the association, biologic gradient/dose response and biologic plausibility.[91]

Based on Dr. Mc Tiernan's review of the totality of relevant evidence including recent studies in the areas of epidemiology, biology, pathology and mechanistic data, it is her professional opinion to a reasonable degree of scientific

[89] *In re J&J*, 509 F. Supp. 3d at 116.
[90] Ex. 47, McTiernan Rep. 25.
[91] *Id*. at 54–56, 96–102.

and medical certainty that the perineal use of talcum product can cause ovarian cancer.[92]

B. Jack Siemiatycki, MSc, PhD

Dr. Siemiatycki is a former tenured Professor of Epidemiology at the University of Montreal and continues in his role as an Adjunct Professor of Epidemiology at McGill University and the University of Montreal.[93] Having retired from his professorship, he remains active in research in various capacities, including various scientific advisory committees, reviewing manuscripts for peer-reviewed scientific journals, mentoring and co-authoring scientific publications.

In addition to writing numerous articles on the causes and assessment of cancer-causing agents, Dr. Siemiatycki chaired the 2006 IARC Monograph panel which evaluated the carcinogenicity of talc not containing asbestiform fibres.[94] Prior to his retention as an expert, he was co-author of a meta-analysis on the association between talc exposure and the risk of ovarian cancer.[95] He has published more than 340 research publications; about one quarter would be considered to have a methodological focus.[96]

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[92] *Id*. at 102.
[93] Ex. 49, Third Amended Expert Report of Jack Siemiatycki, MSc, PhD (May 27, 2024) at 3, Ex. A (Curriculum Vitae).
[94] *Id*. at 4–5.
[95] *Id.* at 5, 26; Ex. 50, Langseth H, Hankinson SE, Siemiatycki J, et al., Perineal use of talc and risk of ovarian cancer, J. Epidem. & Community Health 62(4): 358-360.
[96] Ex. 49, Siemiatycki Rep. at 3.

Dr. Siemiatycki's methodology involved a systematic review of all original epidemiologic published studies, meta-analyses and opinion pieces, experimental toxicology, molecular biology, biologically plausible mechanistic studies, and the IARC Monograph to address the issue of general causation between perineal use of talcum powder products and ovarian cancer.[97] He exercised his expert judgment, examining each study's results, strengths and weaknesses to identify potential sources of error, bias and confounding. As part of his methodology, Dr. Siemiatycki objectively considered the data and scientific literature and performed his own updated meta-analysis.[98] Importantly, the methodology employed by Dr. Siemiatycki to opine on general causation was found to be reliable and admissible by this Court following the *Daubert* hearings and findings in 2020. [99]

Since 2020, Dr. Siemiatycki has amended his report to include newly emerging publications and science relevant to his opinions.[100] These studies include but are not limited to the Woolen meta-analysis and the O'Brien NIH/NCI research studies on talcum powder and ovarian cancer.[101] Having reviewed O'Brien 2024, a study that utilized quantitative bias analysis to take into account various plausible scenarios of multiple sources of errors, it is Dr. Siemiatycki's opinion that

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[97] *Id*. at 30.
[98] *Id*. at 31–33.
[99] *In re J&J,* 509 F. Supp. 3d at 116.
[100] Ex. 49, Siemiatycki Rep. at 30.
[101] *Id*. at 48–49, 63, 69–70.

the observed consistent positive association between talcum powder products and ovarian cancer is unlikely to be explained by any methodologic problems.[102]

Having considered the totality of evidence, which included an evaluation of the data using the Bradford Hill aspects of causal inference, Dr. Siemiatycki concluded that perineal use of talcum powder products can cause ovarian cancer. Based on his contemporary data, his estimated relative risk (RR) between ever-perineal-use of Talcum Powder Products and ovarian cancer is 1.30 (95% CI 1.21-1.40).[103] Based on his meta-analysis of the highest category of cumulative exposure, the meta-RR was 1.39.[104]

C. Rebecca Smith-Bindman, MD

Dr. Smith-Bindman is a Professor of Epidemiology and Biostatistics, Obstetrics, Gynecology and Reproductive Medicine, and Health Policy at the University of California San Francisco School of Medicine, as well as the Director of Radiology Outcomes Research Laboratory.[105] Much of Dr. Smith-Bindman's research is in women's health, including diagnoses of cancers such as ovarian, endometrial, thyroid and breast.[106] She has led research projects funded by more

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[102] *Id.* at 69–70.
[103] *Id*. at 70–71, 81.
[104] *Id*. at 72.
[105] Ex. 51, Third Amended Expert Report of Rebecca Smith-Bindman, MD (May 28, 2024), at 4, Ex. A (curriculum vitae).
[106] *Id*.

than 60 million dollars in research grants, almost entirely focused on cancer diagnosis and prediction, and she has published more than 200 articles.[107] Several of her studies have been systematic, meta-analytic, quantitative reviews of the existing published literature.[108]

In reviewing the medical and scientific literature regarding the relationship between genital talcum powder use and ovarian cancer, Dr. Smith-Bindman applied the same methodology with the same rigor that she uses in her research and clinical practice.[109] She reviewed 49 relevant publications, including 4 cohort studies (5 publications), 11 systematic reviews, 4 pooled data analyses, and 30 case-control studies, as well as numerous review articles and systematic assessments.[110] This review specifically included O'Brien 2020, O'Brien 2024, and Woolen 2022.[111] She examined the strengths and weaknesses of each study, evaluating the potential biases inherent in each.[112]

Dr. Smith-Bindman has performed a thorough and comprehensive analysis of the Bradford Hill causal aspects.[113] In addition, she performed, along with her

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[107] *Id*.
[108] *Id*. at 5.
[109] *Id*. at 3.
[110] *Id*.
[111] *Id*. at 15, 17, 18, 20–23, 27–29, 30–32; Ex. 52, Smith-Bindman Dep. 19:15–42:25, 48:16–60:19; 65:13–83:8; 152:19–153:5; 176:1–186:5; 195:23–196:13; 207:12–212:2.
[112] Ex. 51, Smith-Bindman Rep. at 6, passim.
[113] *Id*. at 33–38.

colleagues from UCSF, a systematic review and meta-analysis, which was published in the peer-reviewed literature (Woolen 2022).[114]

Having performed a Bradford Hill analysis, Dr. Smith-Bindman concluded that the totality of evidence, including literature published after 2020, supports a "strong, positive, and causal association between ovarian cancer and genital exposure to Johnson's Baby Powder and Shower to Shower products. Regular exposure to these talcum powder products causes cancer in some women."[115]

D. Bernard J. Harlow, PhD

Dr. Harlow is currently a Professor of Epidemiology at the Boston University School of Public Health and, for 10 years, was the Mayo Professor and Chair of the Division of Epidemiology and Community Health at the University of Minnesota School of Public Health.[116] Dr. Harlow is an elected member of the American College of Epidemiology and an active member in the Society for Epidemiologic Research, where he served as President Elect, President, and Past-President from 2015 and 2018. For 35 years, he has focused on epidemiologic research specifically in women's cancers and other gynecological disorders. With respect to research on perineal exposure to talc and risk of ovarian cancer, he

[114] *Id*. at 18–32.
[115] *Id*. at 38. *See also* Ex. 4, Woolen 2022.
[116] Ex. 53, Expert Report of Bernard Harlow, PhD and Kenneth J. Rothman DrPh (Nov. 15, 2023), Ex. A; Ex. 54, Addendum to the Expert Report of Bernard J. Harlow, PhD (May 28, 2024).

published four peer-reviewed scientific articles between 1987 and 1999 and a letter to the editor regarding O'Brien 2020 which was answered and published by Dr. O'Brien and colleagues.[117]

Dr. Harlow's methodology involved a systematic review of original epidemiologic published studies (several of which he authored) that addressed the issue of general causation between perineal use of talcum powder products and ovarian cancer.[118] After assessing Bradford Hill factors, noting there is no "checklist" or "recipe" for making causal inference, he assessed whether there were "alternative non-causal explanations to account for the association, including chance, bias or confounding.[119] In assessing the association between talc and ovarian cancer, he considered both the case control and cohort studies, "focusing on potential biases and limitations associated with this research."[120] In addition, he reviewed meta-analyses and pooled studies, focusing on recent high powered studies, including Berge 2017, Penninkilampi 2018, O'Brien 2020, Taher 2020, Davis 2021, and Woolen 2022.[121] He also considered commentaries of other

[117] See *id*. for citations.
[118] Ex 53, Harlow Rep. at 5.
[119] *Id*. at 6–7.
[120] *Id*. at 7–9.
[121] *Id*. at 10–17.

scientists, including those provided by Goodman 2020, Health Canada (2021), and Micha 2022.[122]

In assessing the evidence, Dr. Harlow considered the strength and weaknesses of the case control and cohort studies, including the role of recall bias in the former and nondifferential misclassification bias in the latter.[123] He also considered the biological plausibility of talcum powder causing ovarian cancer. In concluding, he stated that "the consistency of the overall results, combined with biological plausibility that talc acts, similarly to asbestos, as a carcinogen, persuades us that the use of talcum powder products can cause epithelial ovarian cancer in women who use it for feminine hygiene."[124] On May 28, 2024, Dr. Harlow wrote an addendum to his report to address a new study, O'Brien 2024, arising from the Sister Cohort Study, which showed a Hazard Ratio of 1.83 and a positive association that was not likely to be due to recall bias, concluding that "this new analysis adds more evidence to an already large number of studies consistently showing that perineal exposure to talc cam cause ovarian cancer."[125]

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[122] *Id*.
[123] *Id*. at 9, 15, 17–18.
[124] *Id*. at 20.
[125] Ex. 54, Harlow Addendum at 2.

E. Michele L. Cote, Ph.D., M.P.H.

Dr. Cote is a tenured Professor of Epidemiology at the Fairbanks School of Public Health in the Department of Public Health in the Department of Epidemiology at Indiana University in Indianapolis, Indiana.[126] She is also the Director of the Komen Tissue Bank, housed at the Simon Comprehensive Cancer Center (SCCC) at Indiana University. As part of her Directorship, she is the Carrie Ann Glasscock West Endowed Chair in Breast Carcinogenesis. Dr. Cote is a nationally and internationally recognized cancer epidemiologist with primary expertise in female cancers and health disparities.[127] Her research includes publications on gynecologic cancers, including ovarian cancer. She has approximately 155 peer-reviewed manuscripts with an estimated 1/3 of the publications examining ovarian cancer as an outcome.[128]

Dr. Cote's methodology and review focused on her assessment of relevant peer-reviewed epidemiologic, biologic and pathologic literature as well as regulatory, governmental scientific reviews and reports.[129] She then synthesized the data from all lines of evidence utilizing the Bradford Hill viewpoints to determine

[126] Ex. 55, Am. Expert Report of Michele L. Cote, PhD, M.P.H. (May 28, 2024), App'x A (Curriculum Vitae), 3.
[127] *Id*. at 3, 5.
[128] *Id*.
[129] *Id*. at 23, 24.

whether a causal inference could be deduced.[130] Based on the totality of the evidence, Dr. Cote has opined to a reasonable degree of scientific certainty that the genital/perineal use of talcum powder products, including Johnson's Baby Powder and Shower to Shower, can cause ovarian cancer.[131] The basis of her opinion derives from the chemical properties of talc in body powder, elevated measures of effect, most of which are statistically significant when combined into meta or pooled analysis, the pathological evidence, the consistency of results across multiple populations, geographic areas, and in different race/ethnic groups, the evidence of a positive dose-response effect and the plausible biological mechanisms.[132]

In Dr. Cote's amended expert report of May 2024, she considered relevant post-2020 scientific developments. These included, but were not limited to, O'Brien 2020, Davis 2021, Phung 2022, Woolen 2022 and O'Brien 2024.[133] While her review included studies supported by industry scientists, her focus was on original study findings. Much of the new data comes from cohort studies, meta-analysis and international and national scientific and regulatory organizations. Specifically, she examined the recent O'Brien 2024 study concluding that "this

[130] *Id*. at 35, 36.
[131] *Id*. at 6.
[132] *Id*.
[133] *Id*. at 17–18, 21, 24–25.

(O'Brien 2024) is the most thorough analysis of bias examining the association between genital talc use and ovarian cancer. The strong, well-reasoned methodology accounts for potential biases that have been considered potential explanations for the positive associations seen in observational studies."[134]

She concluded that, "[t]he biases that could potentially result in an over or underestimate of the measures of effect did not invalidate the associations seen between use of perineal talc and ovarian cancer risk. A detailed assessment of recall bias and misclassification bias, using cohort data from the Sister Study, provide additional support that the association is not being driven just by these biases."[135]

F. Sonal Singh, PhD

Dr. Singh is an Associate Professor in the Department of Family Medicine and Community Health and the Meyers Primary Care Institute, with a joint appointment in the Department of Quantitative Health Sciences at the University of Massachusetts Medical School. [136] Dr. Singh served as an advisor to the World Bank and the WHO International Agency for Research on Cancer, participating in the WHO-IARC panel, evaluating the carcinogenicity of various drugs and herbal

[134] *Id*. at 25.
[135] *Id*. at 39.
[136] Ex. 56, Expert Report of Sonal Singh, MD, MPH (Nov. 16, 2018) at Ex. A (curriculum vitae), 3–4.

products.[137] He has conducted several epidemiological studies, systematic reviews and meta-analyses featured in prominent medical journals, authoring more than 100 original, peer-reviewed scientific articles.[138]

Dr. Singh's methodology involved a systematic review of the epidemiologic literature and cumulative data to form his opinion concerning Talcum Powder Products' relationship to ovarian cancer.[139] In conducting his analysis, Dr. Singh used a weight of the evidence approach to evaluate all relevant data, including in vitro, animal, and human epidemiologic studies.[140] He analyzed the individual epidemiologic studies for both reliability and validity, noting their strengths and limitations, and specifically evaluating potential biases inherent in all case control and cohort studies. [141] Further, he synthesized and weighed the cumulative body of evidence using the Bradford Hill guidelines of causal inference. Furthermore, he considered confounding factors identified in the studies.[142] Dr. Singh did not say a hazard ratio was strong when it was weak and did not dismiss cohort studies.[143]

In Dr. Singh's Supplemental Expert Reports submitted on November 15, 2023 and May 28, 2024, he considered studies published after his original 2018

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[137] See Singh Rep. at 4.
[138] *Id*. at 5.
[139] *Id*. at 3.
[140] *Id*.
[141] *Id*. at 20–56.
[142] *Id*.
[143] *Id*.

report, including Woolen 2022; O'Brien 2020, and O'Brien 2024.[144] Following his thorough analysis, Dr. Singh arrived at several conclusions, including that there is a statistically significant increased risk of Talcum Powder Products causing ovarian cancer and that the cumulative strength of association ranges from 30% to 60%, which is similar to estimates of other established carcinogens. He further concluded that his opinion is strengthened, further affirmed, and supported by Woolen 2022, O'Brien 2020, and O'Brien 2024. Importantly, the methodology employed by Dr. Singh to opine on general causation was previously found to be reliable and admissible by this Court following an extensive *Daubert* analysis.[145]

G. Patricia Moorman, MSPH, PhD

Dr. Moorman is currently Professor Emeritus in Family Medicine and Community Health at Duke University School of Medicine.[146] Additionally, she has been a member of the Duke Cancer Institute, and for over 25 years, she conducted epidemiological research on ovarian cancer, ovarian function, and women's health issues, with more than 50 publications that relate directly to ovarian cancer.[147]

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[144] Ex. 57, Supplemental Expert Report of Sonal Singh, MD, MPH (Nov. 15, 2023), at 4–7, 10–12; Ex. 58, Second Supplemental Expert Report of Sonal Singh, MD, MPH (May 28, 2024), at 2–7.
[145] *In re J&J*, 509 F. Supp. 3d 116.
[146] Ex. 59, Moorman Dep. 16:24–25, 17:1–9.
[147] Ex. 60, Moorman Dep. 41:6–8.

Her publications include a 2016 study on body powder and ovarian cancer, which reviewed the talc-ovarian cancer association, including plausible mechanisms.[148] In this matter, Dr. Moorman's methodology, detailed in her Reports, included a systemic review of all relevant literature, including original studies, pooled analyses, and meta-analyses. She additionally reviewed documents provided to her during the discovery process.[149] In conducting her analysis, Dr, Moorman incorporated a weight of the evidence approach and applied a Bradford Hill analysis, after examining the strengths and weaknesses of each study, including the internal reliability and study bias of all case control and cohort studies.[150] Further, she considered biases that would both magnify risk and attenuate the risk that would explain the hazard ratio reported in studies.[151] Furthermore, she considered confounding factors identified in the studies.[152] Dr. Moorman did not say a hazard ratio was strong when it was weak and did not dismiss cohort studies.[153] In Dr. Moorman's Second Supplemental Expert Report

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[148] Schildkraut JM, et al., *Association Between Body Powder Use and Ovarian Cancer: The African American Epidemiology Study (AACES)*, 25 Cancer Epidemiology Biomarkers Prev. 1411 (2016).
[149] Ex. 61, Expert Report of Patricia Moorman, MSPH, Ph.D. (Nov. 16, 2018), at 9–11.
[150] *See id*. at 9-11, 38-39.
[151] *Id*. at 9-11, 15-17, 19-25.
[152] Ex. 62, Supplemental Report of Patricia G. Moorman, MSPH, PhD (Nov. 15, 2023) at 3-4.
[153] Ex. 61, Moorman Rep. at 10.

submitted on May 28, 2024, she considered studies published after her original 2018 report, including Woolen 2022; O'Brien 2020, O'Brien 2024.[154]

Following her thorough analysis, Dr. Moorman concluded that genital talcum powder use can cause epithelial ovarian cancer. Importantly, the methodology employed by Dr. Moorman to opine on general causation was previously found to be reliable and admissible by this Court following an extensive Daubert analysis.[155]

H. Daniel Clarke-Pearson, MD

Dr. Clarke-Pearson is a gynecologic oncologist, certified by the American Board of Obstetrics and Gynecology, with more than 40 years of experience treating, teaching, and researching gynecologic cancers, including ovarian cancer.[156] He is a Full Professor at the University of North Carolina-Chapel Hill, Department of Obstetrics and Gynecology; past President of the Society of Gynecologic Oncology (SGO); member of the SGO Ethics Committee; author of over 250 peer-reviewed manuscripts and 50 medical textbook chapters; and editor of three medical textbooks.[157]

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[154] Ex. 63, Second Supplemental Expert Report of Patricia G. Moorman, MSPH, Ph.D. (May 28, 2024) at 3–11.
[155] *In re J&J*, 509 F. Supp. 3d at 116.
[156] Ex. 64, Third Amended Expert Report of Daniel Clarke-Pearson, MD (May 28, 2024), Ex. A (Curriculum Vitae).
[157] *Id*. at 3.

Dr. Clarke-Pearson's methodology included a systemic review of the relevant literature, including peer-reviewed papers, original research, case-controlled studies, meta-analysis studies, systemic analyses, and, contrary to Defendants' allegation, cohort studies. Additionally, he reviewed relevant textbooks and sought additional materials as needed. He "approached this research with the same scientific rigor" he has his "own clinical, academic, and research practice."[158] Grounded in 40 years of knowledge and experience as a gynecologic oncologist, he assessed the data "objectively and critically," considering study strengths and weaknesses by assessing "design, power, reputation of author(s), quality of journal, and potential biases," among other factors.[159] Incorporating a weight of the evidence approach, he assessed the data and information according to its strength, and applied a Bradford Hill analysis.[160] Dr. Clarke-Pearson concluded that "the use of talcum powder products, including Johnson's Baby Powder and Shower-to-Shower, applied to the perineum of women, can cause EOC [Epithelial Ovarian Cancer]."[161]

Judge Wolfson found Dr. Clarke-Pearson's general causation opinions to be reliable and admissible.[162] Since that time, and contrary to Defendants' allegation,

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[158] *Id*. at 4.
[159] *Id*.
[160] *Id*.
[161] *Id*. at 2.
[162] *In re J&J*, 509 F. Supp. 3d at 116.

Dr. Clarke-Pearson has considered newly published studies on genital talc use, including O'Brien 2020, O'Brien 2024 and Woolen 2022. When O'Brien 2024 was published, Dr. Clarke-Pearson specifically amended his expert report to address it.[163] Having fully considered the weight of the evidence, Dr. Clarke-Pearson stated, "The additional studies that have been published and I have considered since my prior report affirm my opinion that the genital use of talcum powder can cause ovarian cancer."[164]

I. Judith Wolf, MD

Dr. Wolf is a board certified gynecologic oncologist, treating women with ovarian cancer and other gynecologic malignancies for more than thirty years.[165] She was a professor at MD Anderson Cancer Center for more than 20 years, a clinical researcher for more than 10 years, and the Chief Medical Officer for two diagnostic companies in the biomedical industry.[166] She has published over 100 peer-reviewed manuscripts, served as principal investigator, co-investigator or collaborator on 11 research grants and numerous protocols, and she has presented at more than 50 conferences.[167]

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[163] Ex. 64, Clarke-Pearson Rep. 10, 13.
[164] *Id*. at 14.
[165] Ex. 65, Third Amended Expert Report of Judith Wolf, MD (May 28, 2024) at 2 and Exhibit A (Curriculum Vitae).
[166] *Id*.
[167] *Id*.

Dr. Wolf's methodology included a systemic review of the relevant literature, including peer-reviewed papers, original research, case-controlled studies, meta-analysis studies, systemic analyses and, again, contrary to Defendants' allegation, cohort studies. Additionally, she reviewed relevant textbooks and sought additional materials as needed. She "approached this issue in a similar way and with the same rigor" she has employed in her "own professional practice, both clinically and in research."[168] Grounded in 30+ years of knowledge and experience as a gynecologic oncologist, she "consider[ed] the reliability and validity of the medical and scientific literature, assessing the evidence according to the strengths and weaknesses of the study under review."[169] Dr. Wolf considered and has been cross-examined on several occasions regarding the possibility of various forms of potential bias as well as potential confounders in the literature. Dr. Wolf formed her expert opinions "using a weight of the evidence methodology in the context of Bradford Hill concepts."[170] She concluded "to a reasonable degree of scientific and medical certainty that Johnson's Baby Powder and Shower to Shower products cause epithelial ovarian cancer in some women. The use of

[168] *Id*. at 2.
[169] *Id*. at 3.
[170] *Id*.

talcum powder products presents a significant risk factor for ovarian cancer in *all* women who use the products."[171]

Importantly, the methodology employed by Dr. Wolf to opine on general causation was found to be reliable and admissible by this Court following an extensive Daubert process.[172] Since that time, and contrary to Defendants' allegation, Dr. Wolf has considered newly published studies on genital talc use, including O'Brien 2020, O'Brien 2024 and Woolen 2022. When O'Brien 2024 was published, Dr. Wolf specifically amended her expert report to address it.[173] Dr. Wolf maintains her opinion that "[w]hen looking at epidemiological studies in their totality, the data demonstrates a consistent, replicated, and statistically significant increased risk of developing epithelial ovarian cancer with perineal talcum powder use."[174]

ARGUMENT

IV. J&J's arguments stemming from the Rule 702 amendments in 2023 are baseless.

Plaintiffs address J&J's law-based challenges—that is, its arguments arising from the amendment to Rule 702—in this section, and leave J&J's challenges based on new science for the next section.

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[171] *Id*. at 23 (emphasis in original).
[172] *See In re J&J*, 509 F. Supp. 3d at 116.
[173] Ex. 65, at 8–9, 19.
[174] *Id*. at 21.

A. J&J seeks what the Court already refused to consider: to have Judge Wolfson's work thrown away and redone.

Defendants' entire bid for a "do-over" of Judge Wolfson's opinion hinges on their assertion that Rule 702 has been amended, and so dramatically that all her work should be jettisoned. In fact, to get the do-over they want, they *have* to make this argument, in light of the Court's pronouncement that it would not "thr[o]w away Chief Judge Wolfson's findings" and did not "intend [] to start *Daubert* motions over from scratch." (ECF No. 32122 at 3.)

The problem is, Defendants spend precious little time showing *how* Rule 702's amendment *did* change the legal standard. Most of their discussion about the 2023 amendment itself is found on pages 31–32 of their memo. That's where they cite one case, *Acetaminophen I*, for the proposition that the rule change "emphasized" something that was already clear to everyone: "that judicial gatekeeping is essential." (Mem. at 32 (punctuation omitted).) Judge Wolfson knew that.

Other cases J&J mentions in its footnoted string cite are equally unremarkable or even inapplicable. One of them is *Sardis v. Overhead Door Corp.*, 10 F.4th 268 (4th Cir. 2021), which J&J says describes the 2023 amendment. That's curious: *Sardis*, a 2021 case that predates the 2023 amendment, does no such thing. Other cases are cited in passing with no analysis. J&J itself offers

nothing of substance to suggest that amended Rule 702 is a major change in the law; perhaps because it isn't.

J&J's challenge to Judge Wolfson's *Daubert* ruling is based on its thin assertion that she "misapprehended" her role as a gatekeeper, which would somehow no longer fly under amended Rule 702. (*E.g.*, Mot. at 2, 33, 66, 81.) One way J&J tries to prove that is by counting up words: J&J says Judge Wolfson "invoked the word 'weight' no fewer than 55 times in her opinion," *id*. at 2, while "the phrase 'preponderance of the evidence' appears just three times in the ruling," *id*. at 33. That's about the deepest J&J's analysis gets. The rest of its argument about Rule 702 being supposedly "misapprehended" or misapplied is an attack on Judge Wolfson's work under even the *former* Rule, which, again, the Court has already determined is out of bounds.

In a similar vein, Plaintiffs next examine the true intent and import of the change to Rule 702, and then show why Judge Wolfson's work stands even after the amendment.

B. Rule 702 was amended in 2023, but the amendment was not intended to change the law or upset decades of settled practice.

Prior to being amended, Fed. R. Evid. 702 read:

> A witness who is qualified as an expert by knowledge, skill, experience, training, or education may testify in the form of an opinion or otherwise if:

> (a) the expert's scientific, technical, or other specialized knowledge will help the trier of fact to understand the evidence or to determine a fact in issue;
>
> (b) the testimony is based on sufficient facts or data;
>
> (c) the testimony is the product of reliable principles and methods; and
>
> (d) the expert has reliably applied the principles and methods to the facts of the case.

Fed. R. Evid. 702 (2022 version) (*available at* https://www.uscourts.gov/sites/default/files/federal_rules_of_evidence_december_1_2022_0.pdf).

After the 2023 amendment, the first clause was amended to add the words "if the proponent demonstrates to the court that it is more likely than not that . . . ." And, Rule 702(d) was amended to state that: "(d) the expert's opinion reflects a reliable application of the principles and methods to the facts of the case."

The idea that expert evidence must, more likely than not, meet the standard of Rule 702 is not a new one. Courts have expressly found that the 2023 amendment "was made to clarify the requirements of Rule 702, not to make substantive changes." *Freeman v. Progressive Direct Ins. Co.*, ___ F. Supp. 3d ____, 2024 WL 2044782, at *3 (D.S.C. 2024). The Advisory Committee Notes to Rule 702 states that these changes were to "clarify and emphasize" what has already long been in the caselaw since (and before) *Daubert v. Merrell Dow*

Pharms, Inc., 509 U.S. 579 (1993), which is that the proponent of expert evidence must demonstrate the expert's ultimate reliability.

J&J says that Judge Wolfson completely ignored the law because her opinion supposedly mentions the word "weight" 55 times which is supposedly proof that she did not follow former or current Rule 702. But, contrary to J&J's insinuation, the rule amendment did not take away the jury's right to place different weight on expert opinions. "For example, if the court finds it more likely than not that an expert has a sufficient basis to support an opinion, the fact that the expert has not read every single study that exists will raise a question of weight and not admissibility." (Advisory Committee Notes.) The Notes emphasize that the decision to determine admissibility rests where it long has: with the judge.

C. Judge Wolfson followed Rule 702 as it was written then and her decision is no less correct under today's Rule 702.

Judge Wolfson knew this. She wrote, right in her opinion, that "trial courts must perform a gatekeeping function to ensure the relevance and reliability of expert testimony." *In re J&J*, 509 F. Supp. 3d at 130. Despite what J&J says, Judge Wolfson knew that Rule 702—former Rule 702—required Plaintiffs to "demonstrate by a preponderance of evidence that their [experts'] opinions are reliable." *Id*. at 187 (citing *In re Processed Egg Prods. Antitrust Litig.*, 81 F. Supp. 3d 412, 416 (E.D. Pa. 2015)).

Judge Wolfson went on to hold that courts "are to consider all aspects" of expert opinion, including "the methodology." *Id*. at 131. She held that courts must also "ensure that expert testimony reflects accepted standards within the relevant scientific . . . communities." *Id*. She went on for almost two pages in detail about her specific duty to examine methodology in particular. *Id*. at 131–32.

Not only did she examine her general duty to evaluate reliable methodologies, she discussed the application of the Bradford Hill factors. She noted that Bradford Hill's approach "is a reliable method for determining causation." *Id.* at 161 (citing *In re Roundup Prods. Liab. Litig.*, 390 F. Supp. 3d 1102, 1130 (N.D. Cal. 2018)). But she didn't just blindly admit any expert claiming to do a Bradford Hill-style analysis; she went on to note the Third Circuit's admonition that, "despite the fact that the methodology is generally reliable, each application is distinct and should be analyzed for reliability." *Id*. (citing *In re Zoloft (Sertraline Hydrochloride) Prods. Liab. Litig.*, 858 F.3d 787, 795 (3d Cir. 2017)). She mentioned *Zoloft*'s requirement that Bradford Hill techniques must be both reliable and reliably applied.

Judge Wolfson then went on to review the reliability of each expert's assessment of *each* of Sir Bradford Hill's nine factors. This analysis ran for over twenty pages, *id*. at 162–85, and there is a specific section on each of them where

she analyzes the evidence and methodology. *E.g.*, the strength-of-association factor is at *id*. at 162–68, the consistency factor at 168–72, and so on.

Two points will suffice to dispose of J&J's challenges based on the Rule 702 amendments.

First, nothing Judge Wolfson did runs afoul of amended Rule 702 (which is the only challenge the Court said it would hear), because amended Rule 702 envisioned exactly this kind of gatekeeping. The amended rule (and its Advisory Committee Notes) show a concern that judges not leave the admissibility determination for the jury. Judge Wolfson assuredly made that determination for herself. She specifically found that Plaintiffs had met their burden of proof, establishing their experts' admissibility beyond a preponderance of the evidence.

And second, none of this work depicts a renegade judge who has abdicated her duty to assess reliability of experts' methodology. Of relevance here, Judge Wolfson actually excluded some of the opinions of Plaintiffs' experts, Dr. Ghassan Saed, as to his general causation opinions (but not others). *Id*. at 136–40. Judge Wolfson's cannot truly be as reckless as J&J insinuates, or she would not have acted as such a gatekeeper with this expert.

Judge Wolfson painstakingly followed in the footsteps of each expert's path and checked that that expert reliably applied reliable scientific methods.

At the end of the day, J&J does not *really* press very hard on the notion that she didn't. J&J really just appears to be using the Court's April 30 order and the minor amendment to Rule 702 to get an improper "do-over" of the entire *Daubert* question. J&J's motion, to the extent it is based on the amendment to Rule 702, should be denied.

V. The new science post-2020 strengthens Plaintiffs' experts' opinions.

The Court's other basis on which parties were permitted to challenge Judge Wolfson's decision was if "new science is shown to directly contradict or challenge Chief Judge Wolfson's previous findings." (ECF No. 32122 at 6.)

There has been new, affirmative scientific evidence, but it does not contradict those findings. In fact, since 2020, there have been scientific studies published by independent researchers, national organizations, and international scientific bodies, and those studies support Plaintiffs' experts' opinions. They have concluded that talc, both with and without asbestos, ***can cause*** ovarian cancer.

One of those new statements is the IARC reclassification of talc, that *alone* probably causes ovarian cancer, and talc *with asbestos* definitely does so.[175] Other important new developments come from cohort studies, which have now been

[175] Ex. 44, Fidalgo, *Talc is classified as "probably carcinogenic to humans" by the IARC*, Science Media Center Spain (May 7, 2024).

focused on exploring the talc/ovarian cancer link in a way they previously have not been used.

The basis for Plaintiffs' expert's opinions remains the same as it was in 2019—that talcum powder is capable of causing epithelial ovarian cancer because:

- Talcum powder generally, and J&J's products specifically, contain known carcinogens, including asbestos, fibrous talc, and heavy metals.
- There is a consistent association, across decades of epidemiologic studies of different designs and with different researchers involving different patient populations that have demonstrated genital talc use is associated with a risk of epithelial ovarian cancer.
- The increased risk of epithelial ovarian cancer seen in these studies is between 30–60%.
- There is evidence of a dose-response relationship, because risk increases with both frequency and duration of genital talc use.
- It is biologically plausible that genital talcum powder causes ovarian cancer based upon evidence that talcum powder can migrate from the perineal area, through the open female genital tract, and reach the fallopian tubes and ovaries where it can create an inflammatory response.

With respect to scientific studies, the vast majority of new, post-2020 evidence comes from prospective cohort studies—the very types of studies that Defendants' experts previously argued to Judge Wolfson were the most appropriate studies to evaluate the association between genital talc use and ovarian cancer.[176]

The post-2020 cohort studies can be summarized as follows:

[176] 509 F. Supp. 3d at 162 ("Defendants further fault Plaintiffs' causation experts for relying primarily on case-control studies, as opposed to cohort studies, which Defendants maintain provide more reliable results.").

- **Strength of association.** The new cohort study data, primarily from independent scientists at National Institutes of Health (NIH), shows a positive association between talc use and cancer in all women, with a statistically significant association in women with an open genital tract and frequent and long-term users.[177] These findings provide further support for the 1.2–1.4 (20-40%) relative risk range from other studies Judge Wolfson had in the record.

- **Consistency of association.** The post-2020 studies, on the whole support the consistency-of-association factor for causation. According to one study, O'Brien 2024, these recent studies were "consistent with previous studies, pooled analyses or metanalysis of case control studies that have produced odds ratios of 1.2 to 1.4,"[178] as well as a "positive association" in a 2020 pooled analysis the NIH scientists conducted "of prospective cohort studies."[179]

  And as the NIH itself has noted, there is now a "[p]ersistent positive association between genital talc use and ovarian cancer."[180]

  Previously, Judge Wolfson noted that the cohort studies were positive, but not statistically significant, a fact that has changed since 2020. This is further support for Judge Wolfson's position that there is reliable evidence on the "consistency" Bradford Hill factor. *In re J&J*, 509 F. Supp. 3d at 168–72.

- **Dose-response relationship.** There is new evidence from cohort studies that further strengthens support for this Bradford Hill factor. As the O'Brien 2024 authors noted, evidence from cohort data demonstrated that the risk increased, from 1.81 to 2.01, in women who used genital talc more frequently and for longer durations.[181] This finding was confirmed

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[177] Ex. 1, O'Brien 2020; Ex. 2, O'Brien 2024 ("The association between genital talc use and ovarian cancer was higher for frequent, 1.81 [], and long-term users, 2.01 [], compared with never users."); Ex. 6, Stayner at 2 ("more consistent positive associations between associations for ever-use versus never-use have been reported in pooled cohort studies and case-control studies").
[178] Ex. 2, O'Brien 2024 at 13.
[179] *Id.* (citing O'Brien 2020).
[180] Ex. 8, NIH/NIEHS Environmental Factor, at 2.
[181] Ex. 2, O'Brien 2024.

by NIH, which summarized that evidence and stated the "strongest associations [were] observed for frequent and long-term users and for use during reproductive years."[182]

Further, a pooled cohort study found a 1.4 increased risk for daily users in an analysis of Nurse's Health Study cohort data and an overall risk of between 31% and 65% for frequent use across all combined studies.[183]

- **Biological plausibility.** Additional evidence that it is biologically plausible for talc to cause ovarian cancer has accumulated since 2020. NIH scientists have now determined that talc *can* migrate, and "once deposited onto epithelial cells, it can cause chronic inflammation, leading to a series of mutagenic events, and this effect is worse in talc contaminated with asbestos, a known carcinogen."[184]

  Also, since 2020, the Environmental Protection Agency (EPA) has noted three separate times that asbestos can be present in talc and that it is a human ovarian carcinogen.[185] Related to these scientific events is the July 2024 decision by the International Agency for Research on Cancer (IARC) to reclassify talc as a "Category 2A"probable carcinogen, based in part on the "strong mechanistic evidence that talc exhibits . . . including inducing chronic inflammation and altering cell proliferation, cell death, or nutrient supply."[186]

Each of these factors is discussed in greater detail its own section below.

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[182] Ex. 8, NIH /NIEHS Environmental Factor at 2; Ex. 66, ASCO Press Release, *Study Finds Association Between Genital Talc Use and Increased Risk of Ovarian Cancer* (May 15, 2024).
[183] Ex. 4, Woolen 2022.
[184] Ex. 67, Kemi Ogunsina, et al., *Association of genital talc and douche use in early adolescence or adulthood with uterine fibroid diagnoses*, 229 Am. J. Obst. & Gyn. 665 (Dec. 2023).
[185] See note 33 above.
[186] Ex. 6, Stayner 2024.

A. Strength of association: New post-2020 study evidence further supports the strength of the association.

The "strength of association" factor considers the relative risk, meaning the "ratio of the incidence rate of disease in exposed individuals to the incidence rate in unexposed individuals." *In re J&J*, 509 F. Supp. 3d at 162.

The most relevant evidence for this factor is of course the epidemiologic studies: case-control studies, cohort studies, and meta-analyses/pooled studies.

Plainly, the O'Brien 2020, O'Brien 2024, Woolen 2022, Chang 2024, and Davis 2021 studies are all compelling new, confirmative evidence that supports a strong association between talcum powder in the genital tract and ovarian cancer. They are discussed in detail in Section II-B above. But in summary, the O'Brien 2020 authors found a positive, statistically significant association in women with patent reproductive tracts of 1.13. O'Brien 2024, the most recent study and one that resolved longstanding data collection issues from the Sister Study and found a statistically significant 1.82 increased risk that went up even more with long-term use, establishing both a strong association and a dose-response relationship. Woolen 2022 involved pooled data that showed an odds ratio of 1.47. Chang 2024 observed a risk of 1.06 in once a day users and 1.26 in five-days-a-week users. (That study also showed a dose-response relationship.) And Davis 2021 saw a statistically significant 30-35% increased risk.

Thus, the post-2020 evidence of an association has only grown. Far from constituting scientific evidence that "directly contradict[s] or challenge[s] Chief Judge Wolfson's previous findings," the evidence buttresses Plaintiffs' experts' views—and there is no reason to revisit those findings.

J&J's response to this robust, consistent new data has been to attempt to explain it away. But these studies add to the already robust body of literature on strength of association in the range of 1.2–1.6, based on data from *both* prospective and retrospective studies, with a higher risk of association for long term and frequent users of talcum powder.[187] They further confirm that recall bias—the explanation J&J has given for all the studies—is not the likely explanation. Rather, the increasingly clear explanation is the one that Plaintiffs' experts and health authorities have reached: there is an association between talcum powder and epithelial ovarian cancer.

[187] Because of the association, medical literature has consistently referred to genital talc powder as a "risk factor" for ovarian cancer. Ex. 68, Hunn and Rodriguez, *Ovarian Cancer: Etiology, Risk Factors, and Epidemiology*, 55 J. Clin. Obstretrics and Gyn. 3, 12 (2012) ("[E]vidence demonstrating . . . an increased risk"); Ex. 69, Wu, *African-Americans and Hispanics remain at lower risk of ovarian cancer than non-Hispanic Whites after considering non-genetic risk factors and oophorectomy rates*, 24 Cancer Epidem. Biomarkers Prev. 1094 (July 2015) (genital talcum powder use is a monogenetic risk factor for epithelial ovarian cancer); Ex. 10, Phung 2022, at 4 (genital talc use is a "well-established risk factor" for epithelial ovarian cancer).

In their updated reports, each of the PSC's causation experts took the new data into account and explained how it supported their opinions. (Please see Section III above.)

Several points made by Defendants can be refuted.

1. J&J must now accept that there is strong and consistent epidemiological data from multiple study designs.

J&J is caught in a logical trap of its own devising. Defendants' pre-2020 scientific argument against the epidemiological evidence was simple and mechanical: while case-control epidemiologic studies and meta-analyses of epidemiologic studies *did* show that genital talc was associated with a 1.2–1.6 increased risk, the prospective cohort studies did not. Defendants then argued that, on the supposed "hierarchy of . . . studies," case-control studies were lower than cohort studies, so that the case-control studies were effectively cancelled out. *Id*. at 165.

Now that there is strong and consistent data—from the cohort studies J&J found wanting in 2020—J&J is forced to accept that the scientific picture has shifted in favor of Plaintiffs.

2. J&J again attempts to disclaim the evidence as methodologically "weak," which Judge Wolfson already rejected.

In the motion at bar, J&J also complains that Plaintiffs' experts have argued the association from the studies is strong, when it is actually weak in J&J's view.

(Mem. at 40.) According to J&J, this highlights the unreliability of plaintiffs' experts. J&J further argues, as it already did in 2019, that Plaintiffs' experts also ignored evidence of recall bias and confounding which would further lessen the observed risks. *Id*. at 40–47.

But a semantic debate over whether the 30–60% increased risk seen in both the case-control studies and the cohort data is "small," "moderate" or "strong" is as much a red herring today as it was in 2019. As the Reference Manual on Scientific Evidence makes clear: "While strength is a guideline for drawing an inference on causation from association . . . there is no specified threshold required."[188] This point is also supported by basic textbooks on epidemiology: "[A] strong association is neither necessary nor sufficient for causality, and [] weakness is neither necessary nor sufficient for absence of causality." [189] That textbook cites, as examples, links between "smoking and cardiovascular disease or between environmental tobacco smoke and lung cancer [which are] accepted by most as causal even though the associations are considered weak." *Id*.

Judge Wolfson held that whether the relative risk found "can be categorized as 'strong' or 'weak' is best left to the jury." 509 F. Supp. 3d at 164. Her focus, in judging the admissibility of that evidence, was "whether the experts used a sound

[188] Reference Manual on Scientific Evidence 611, n. 186 (emphasis added).
[189] Ex. 15, Rothman, *Modern Epidemiology*, at 15.

methodology in reaching their conclusion that the relative risk range of 1.2 to 1.6 demonstrates a risk association." *Id*. With the semantic argument aside, one thing is now clear that was disputed in 2020—there is indeed an association, across all study designs, including cohorts.

Outsiders agree. In its final causation assessment in 2021, Health Canada considered the "strength of association" factor and, like Judge Wolfson, found reliable evidence that it had been satisfied:

> Strength of association is typically a consideration of the relative risk (or OR) between the chemical exposure and the disease. A large risk increases confidence of a causal relationship; however, risks of lower magnitude do not preclude a positive association and rather, may represent a low level of exposure or a rare disease (Hill 1965; Cogliano et al. 2004). The pooled ORs from available meta-analyses ranged from 1.22 to 1.35 (Huncharek et al. 2003; Langseth et al. 2008; Terry et al. 2013; Berge et al. 2018; Penninkilampi and Eslick 2018; Taher et al. 2019), which would not be considered "large." However, the results for the pooled analyses are statistically significant, with narrow confidence intervals. As noted in Table 7-1, a high proportion of available case control studies representing a broad section of the population have reported strikingly similar ORs. Ovarian cancer is recognized as a rare disease (AICR 2020; CTFPHC 2020; NCI-SEER 2020) and, as such, the large number of studies giving similar results is noteworthy.

After considering arguments made by J&J, its litigation experts (Diette and Merlo), and Plaintiffs' experts (McTiernan, Moorman, Siemiatycki, Singh, and Smith-Bindman), Health Canada concluded that the burden had been met:

> Strength and consistency of association are two factors often considered together. The replication of results seen across multiple studies supports strength (Singh 2018). The measured ORs (1.22 to 1.31) are modest, but they are also similar and unlikely to be random. Considering that ovarian cancer is rare, and therefore that a large data set is required to detect an association, the findings in the available literature are significant.

3. A 2.0 increased risk ratio is not necessary to find causation.

Plaintiffs' experts determined that the association ranging between 1.2–1.6 was strong enough to support an assessment of causality. Contrary to J&J's argument,[190] it is not necessary in science to find a risk above 2.0 to find an important causal association. There are many instances of established causal relationships where the association is under 2.0, and yet scientists find causality. Some of these appear in Table 12 of Dr. Siemiatycki's report (Ex. 49 at 101). That table is replicated below:

Agent	Disease	Approximate HR
Urban air pollution	Lung cancer	1.09
Trichloroethylene	Kidney cancer	1.32
Diesel engine emissions	Lung cancer	1.42
Benzene	Leukemia	1.72
Domestic radon gas	Lung cancer	1.29
Second hand cigarette smoke	Lung cancer	1.64
Intermittent intense sun exposure	Melanoma of the skin	1.61
Estrogen-progestin menopausal therapy	Breast cancer	1.59
Cigarette smoking	Cardiovascular disease	1.6

[190] Mem. 9, 36; *see also In re J&J*, 509 F. Supp. 3d at 163.

Agent	Disease	Approximate HR
Physically inactive (compared with physically active)	Hypertension	1.19
Physically inactive (compared with physically active)	Diabetes	1.12
Low fruit and vegetable diet	Cardiovascular disease	1.09

All of these links are established causal relationships in science.

J&J intimates through its argument that outside investigator don't use the word "cause" or "causal" to describe the associations they detected, so that is proof that there is no consensus. And J&J asserts that when Plaintiffs' experts say the relationship is causal, they must be improper advocates. Neither proposition is correct. The reason why words like "cause" are not typically used is much more benign: it is typically against journal policy to do so based on the results of a single study. *E.g.*, Ex. 70, Dahabreh, *Causal Inference About the Effects of Interventions From Observational Studies in Medical Journals*, 331 JAMA 1845 (May 9, 2024). That does not bar Plaintiffs' experts from looking at the evidence as a whole and drawing a conclusion—nor does it bar Defendants' experts from finding "no cause" either.

4. Plaintiffs' experts considered recall bias and confounders.

Through cherry-picking quotes and selective editing, J&J suggests that Plaintiffs' experts failed to consider that recall bias or confounding variables

(including douching practices) might be behind the fifty years of consistent observational data, rather than an actual relationship. (Mem. 41–47.)

But that isn't a new argument. J&J made the exact claim before Judge Wolfson, who held, "I do not agree that plaintiffs' general causation experts failed to consider issues of confounding and recall bias." *In re J&*J, 509 F. Supp. 3d at 166. Plaintiffs' new reports are consistent with that assessment.[191]

* * *

In conclusion, the evidence on the "strength-of-association" factor is more than sufficient to continue to support Plaintiffs' experts' opinions.

B. Consistency of association: New post-2020 cohort study evidence supports a finding of consistency among all the studies

As Judge Wolfson noted, "[t]he consistency factor considers whether the results of the relied upon studies have been replicated." *In re J&J*, 509 F. Supp. 3d at 168. Previously, Defendants' argument against consistency centered on a claim that is not much different than their claim about the strength of association:

> . . . Defendants contend that the epidemiological studies are not, in fact, consistent, in that the cohort and case-control studies have reached different results. . . . In other

[191] For experts' discussion and analysis of recall bias and confounding, *see* Ex. 55, Cote Rep. 7–8, 17–20, 22–26, 28–29, 31–32, 36, 39; Ex. 64, Clarke-Pearson 3d Am. Rep. 10, 13; Ex. 54, Harlow Rep. Addendum 1–2; Ex. 53 Harlow Rep. 17–18; Ex. 47, McTiernan 3d Am. Rep. 12, 17, 21–22, 27, 28, 48, 50–54, 56, 62, 76, 77, 79, 81, 97, 98; Ex. 63, Moorman 2d Supp. Rep. 2, 6–11, 14–15; Ex. 49, Siemiatycki 3d Am. Rep. 54, 62, 63; Ex. 58, Singh 2d Supp. Rep. 1–5; Ex. 51, Smith-Bindman 3d Am. Rep. 16–17, 19, 22; Ex. 65, Wolf 3d Am. Rep. 6, 8, 11.

> words, Defendants argued that because no cohort study concluded there was a statistically significant association between talc use and ovarian cancer, the two types of studies cannot be consistent.

As Judge Wolfson held, there was adequate evidence of consistency in 2020, even though the three cohort studies available at the time did not clearly show an association that was statistically significant. *Id*. at 168–70. She acknowledged that plaintiffs experts provided good reasons for this, which included: the small number of ovarian cancer cases in the individual cohorts (that they were "underpowered"), the lack of adequate follow-up (to account for "latency") and the fact that none of the cohort studies was actually designed to look at the question (raising issues of misclassification bias which would mask a true association). *Id*.

But the same is not true any more. There is consistency between the various studies based on the new cohort data that both expands the power by pooling cohort studies (O'Brien 2020) and which measures lifetime talcum powder exposure with longer follow up time (O'Brien 2024). Now, it is J&J that wants to ignore statistically significant results, including the results of O'Brien 2020 and O'Brien 2024, in favor of non-significant ones.

1. The post-2020 "new science" confirms a consistent association among the case-control studies, meta-analyses, and cohort studies.

This consistency between the case-control data and the cohort data has been observed numerous times and described in numerous settings since 2020. Indeed,

in its 2021 Bradford Hill causation analysis, Health Canada explicitly considered the views of J&J and its litigation experts on the consistency factor, and concluded the consistency factor had been met stating that "there is a high degree of consistency in the epidemiological studies across several decades conducted in different parts of the world."[192]

And that's not all. The NIH authors of the post-2020 cohort studies themselves also agree that there is consistency between case-control and cohort data. For example, in her response to a *Letter to the Editor* regarding the correct interpretation of her 2020 study, Dr. O'Brien commented that the result of the case-control and cohort studies was consistent with a "true association that may be somewhere in the middle" between 8% and 35%.[193] As Dr. O'Brien stated, when agreeing with Dr. Harlow in that letter: "We never equated the lack of statistical significance to evidence of no association."[194]

A finding of consistency in the data was also observed in Wentzensen 2021, where the data from cohort, case-control studies, and meta-analyses was exhaustively reviewed. The authors concluded that "Overall these results . . . demonstrate that there *is* a positive association between talc and serous ovarian

[192] Ex. 5, Health Canada 2021 at 33.
[193] Ex. 38, O'Brien et al., Letters to the Editor, 323 JAMA 2095, 2097 (May 26, 2020).
[194] *Id.*

cancers . . . .” *Id*. at 7 (emphasis added). This consistent association, they added, “support the hypothesis that the positive association between genital powder and ovarian cancer may be limited to women with patent reproductive tracts.” *Id*. at 8.

The NIH and the National Institute of Environmental Health Sciences also found that the evidence of a positive association is consistent with other literature and points in the same direction. In announcing O’Brien 2024, for example, they wrote that it offered “compelling evidence” that shows a “consistent association between genital talc use and ovarian cancer.”[195] The 2024 study itself points out the “consistency” between its results, the O’Brien 2020 pooled cohort data, and the talc case-control studies:

> Our findings of a positive association between genital talc use and ovarian cancer are **consistent** with previous studies. **Pooled analyses or meta-analyses of case-control studies have** produced odds ratios of 1.2-1.4.The HR from **a pooled analysis of prospective cohort studies** [in O’Brien 2020] also indicated a positive, albeit small association (HR 1.08), and as previously noted, this effect estimate is likely biased toward the null because of nondifferential misclassification of exposure.[196]

In July 2024, IARC Working Group found the same. They examined talc and ovarian cancer and reached a similar conclusion about consistency between case-control and cohort studies. It noted that since 2006, “more consistent positive

[195] Ex. 8, NIH/NEIHS Environmental Factor at 1.
[196] Ex. 2, O’Brien 2024 at 14.

associations for ever-use versus never-use have been reported in pooled cohort studies and case control studies, including evidence of the exposure-response relationship with frequency or duration of use."[197]

In short, while Judge Wolfson found sufficient evidence of consistency across study designs of all types in 2020, the scientific record is even stronger and better described in 2024. Nothing in the new science rebuts her existing findings.

2. J&J's renewed *Daubert* challenge rests on the discredited view of "significance testing" already addressed by Judge Wolfson; a view rejected by the American Statistical Association (ASA), and which is described in the *Reference Manual* as unsophisticated.

To repel the post-2020 assessments of consistency described by all of these authorities, J&J attempts to manufacture "inconsistency" in the evidence.

There *are* statistically significant results relating to women with patent tubes in O'Brien 2020, and *there are* statistically significant results overall in O'Brien 2024. J&J cannot ignore these findings.

However, J&J attempts to discredit the positive overall results from O'Brien 2020 (1.08, CI 0.99–1.17), a group that includes women with closed reproductive systems—just because the confidence interval barely overlapped with 1.00. Doing so then allows J&J to urge that there is not consistency in the statistical findings

[197] Ex. 6, Stayner, at 2.

because this finding from O'Brien 2020 isn't "consistent" with the other positive findings.

What the parties really have between them, as Judge Wolfson found, is "a dispute over the role that statistical significance plays in determining the consistency of epidemiological studies." *Id*. at 169. While this issue can bleed into the "strength-of-association" factor, Judge Wolfson deftly addressed the dispute in the context of the "consistency factor." *Id*. at 169–70. So did J&J, Mem. 58–64, so Plaintiffs respond under the consistency factor too.

J&J—while denying that it has "never argued that statistical significance is a litmus test for consistency," *id*. at 62—nevertheless does urge that Plaintiffs' experts are employing an unreliable methodology because they "selectively rely on statistical significance" at times, *id*. at 63, but otherwise "retir[ed] the longstanding concept of statistical significance," *id*. at 64.

The centerpiece of J&J's consistency claim, as it was before, is simple: Plaintiffs' experts should "significance test," *i.e*., to sort the talc observational studies according to statistical significance alone. According to J&J, the PSC's experts erred methodologically by failing to perform a mechanical multiple-choice "significance—yes" and "significance—no" exercise—also called "significance testing" in the epidemiologic literature. *E.g.*, 509 F. Supp. 3d at 181. Under that

rubric, results could be consistent only when there is a perfect line-up of "yes" answers. This has been soundly rejected.[198] It should be rejected again.

It is true that there has been a long tussle in the academic world, and observed by the courts, over the value of the concept of statistical significance. However, J&J is on the losing side of it, and the modern trend is to take statistical significance into account without rigidly excluding all studies that are not statistically significant.

In 2019, the American Statistical Association (ASA) rejected the use of "significance testing" outright. The entire March 2019 supplemental volume to the ASA's journal, *The American Statistician*, discusses the persistent misuse of statistical significance as a metric for assessing an association.[199] This publication was accompanied by an important editorial, with over 800 signatories, on the problems with statistical significance.[200] One of the authors of that article was Dr. Sander Greenland, a prominent epidemiologist who is cited in the Reference Manual as authoritative.

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[198] Ex. 15, Rothman, *Modern Epidemiology*, at 25; Ex. 71, Rothman, *Six Persistent Research Misconceptions*, 29 J. Gen. Intern. Med. 1060, 1060 (2014); Ex. 72, Ronald L. Wasserstein, et al., *Moving to a World Beyond "p<.05"*, 73 The American Statistician 1 (Supp. 1 2019); Ex. 73, Amrhein, Greenland, & McShane, *Retire statistical significance*, 567 Nature 305 (2019).

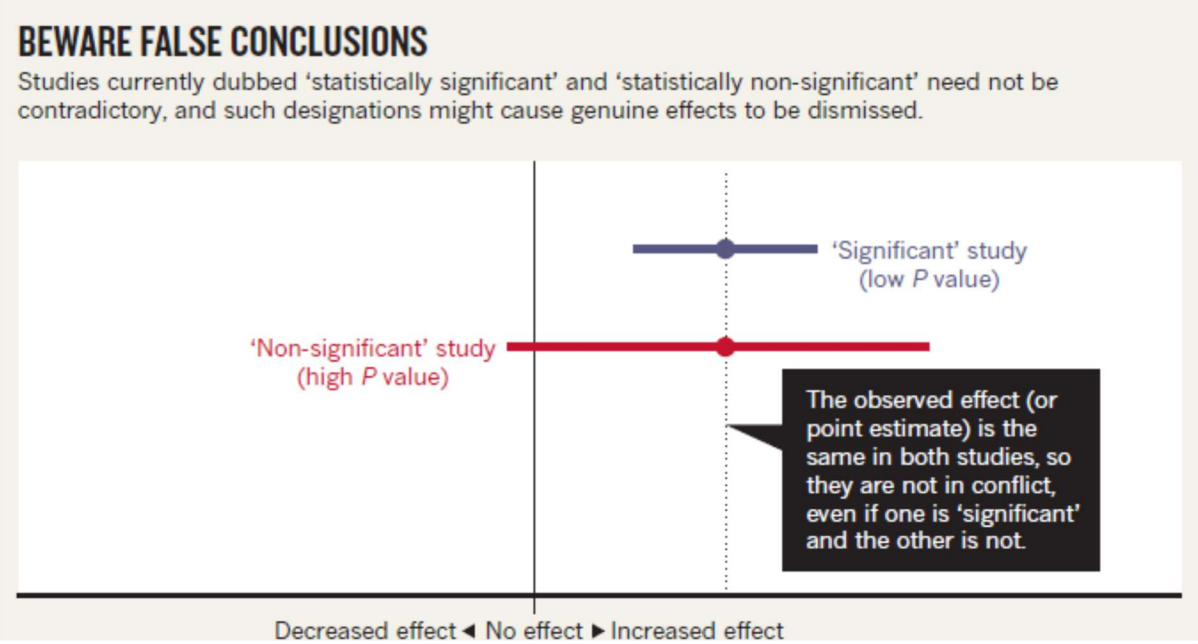
[199] 73 The American Statistician 1 (Supp. 1 2019), *available at* https://www.tandfonline.com/toc/utas20/current.

[200] Ex. 73.

The authors wrote:

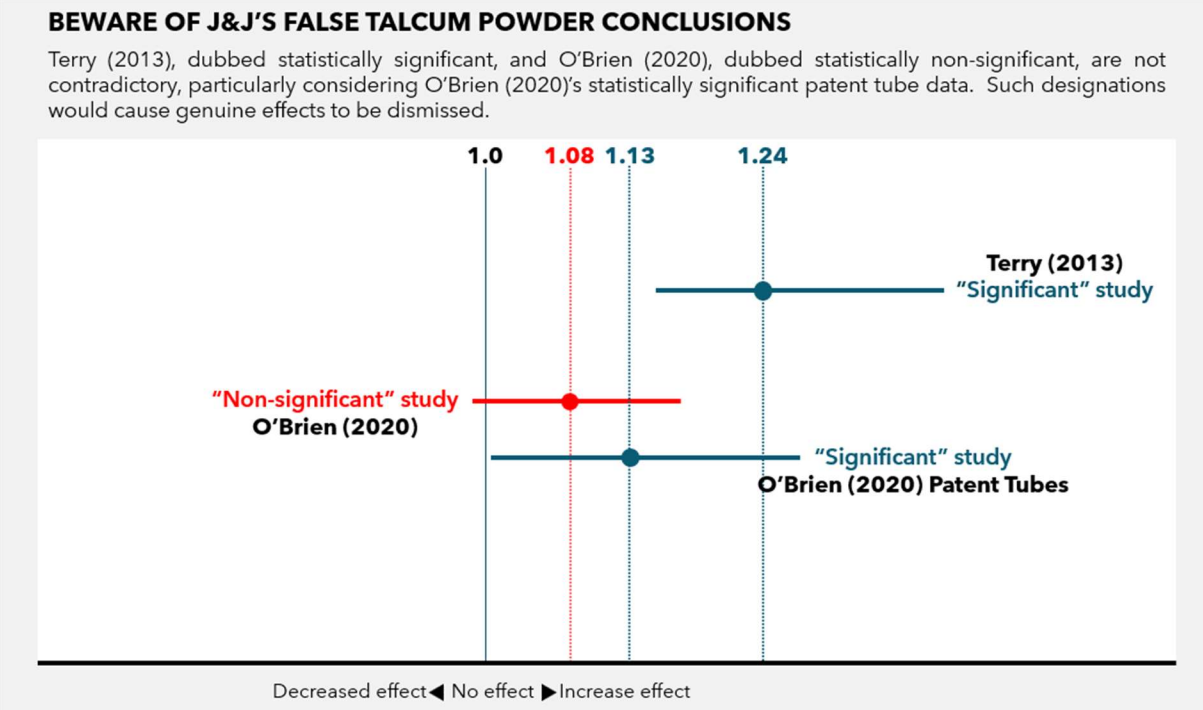
> Let's be clear about what must stop: We should never conclude that there is 'no difference' or no association' just because a p value is larger than a threshold of .05 or equivalent because a confidence interval includes zero. **Neither should we conclude that two studies conflict because one has a statistically significant result and another did not. These errors waste research efforts and misinform policy decisions.**[201]

To illustrate his point, Dr. Greenland provided the following example that is on point with how J&J compared the results of the Talc case-control Data with the O'Brien 2020 Pooled study:



In this case, the chart comparing the Terry pooled study of case-control Data with the O'Brien 2024 pooled study of Cohort data and the data on Patent Tubes reveals a very similar table.

[201] *Id*. (emphasis added).



Other important journals are in accord. The New England Journal of Medicine, for example, issued publication guidelines in 2019 regarding statistical significance. It wrote that NEJM editors and statistical consultants have become "increasingly concerned about the overuse and misinterpretation of significance testing and p values in the medical literature."[202] And in 2024, the Annals of Internal Medicine ran a particularly blunt editorial, also rejecting the statistical significance dichotomy that J&J urges. The authors noted that the "deficiencies of statistical significance testing . . . have been emphasized for decades."[203] They

[202] Ex. 74, Harrington et al., *New Guidelines for Statistical Reporting in the Journal*, 381;3, 285 (Jul. 18, 2019).
[203] Ex. 75, Savitz et al., *Responding to Reviewers and Editors About Statistical Significance Testing*, Annals Intern. Med. (Feb. 20, 2024).

particularly noted the inappropriate "dichotomization of results that are on a continuum" and "inaccurate interpretation of results that are not statistically significant as supporting the null."[204]

These concerns among the academy have long been reflected in judicial cases. *In re TMI Litig. Cases Consol. II*, 922 F. Supp. 997, 1017 (M.D. Pa. 1996) ("there is presently an ongoing dialogue within the relevant scientific community on the issue of significance testing. Moreover, the court is aware that the debate has carried over into the judicial arena."). The Third Circuit "decline[d] to state a bright-line rule," noting that statistical significance should not be understated or overstated. *In re Zoloft*, 858 F.3d at 793. And the 2011 Reference Manual's Guide on Epidemiology notes that "[e]pidemiologists have become increasingly sophisticated in addressing the issue of random error and examining the data from a study . . . without the necessity of rejecting all studies that are not statistically *s*ignificant." (Ref. Man. Sci. Evid. 579.)

J&J, however, ignores all this. It ignores the binding *Zoloft* opinion—giving no "bright-line rule"—in favor of an out-of-Circuit district court opinion that was not approved, *In Re Acetaminophen I*, to suggest the opposite. (Mem. at 62–63.)

However, J&J's defective arguments on statistical significance were rejected before—by Judge Wolfson, when there were no statistically significant results from

[204] *Id*.

the cohort studies. 509 F. Supp. 3d at 170–71 (approving expert who "gave weight to positive, non-significant results where such weight was warranted"); *id*. at 170 (citing *In re Zoloft*, 858 F.3d at 793 ("A causal connection may exist despite the lack of significant findings . . . A standard based on replication of statistically significant findings obscures the essential issue: a causal connection.").

Nothing in the science of statistics has changed since 2020 to upend Judge Wolfson's findings permitting Plaintiffs' experts, when appropriate and in context, to rely on studies that are not strictly statistically significant. Further, nothing in any of the science should upend her finding that the "consistency" Bradford Hill factor is met. Indeed, the Court has all the more reason to reject J&J's rehashed argument now that the positive association seen in O'Brien 2020 is now coupled with reliable, statistically significant data from newer cohort studies.

4. It is J&J and its causation experts, not Plaintiffs' causation experts, who ignore statistical significance in the post-2024 talcum powder studies.

While plaintiffs would have preferred that Judge Wolfson strike J&J's Experts who relied on that discredited "Significance testing" methodology, she did not do so. Rather, she allowed both sides to explain their methodology to the jury. *In Re J&J*, 509 F. Supp 161, 189. But to be clear, Plaintiffs' experts and the O'Brien scientists, IARC, Health Canada, and others are advocating a correct

conclusion based in current reliable statistical methodology, while J&J and its experts push a false one.

Previously, J&J argued that Plaintiffs' causation experts "ignore the statistically insignificant nature of purported positive results from cohort studies." 509 F. Supp. 3d at 169. In 2020, Judge Wolfson disagreed stating that plaintiffs' experts provided "detailed reasons for their findings and their approach considering statistical significance…" Id at 170. There is nothing in plaintiff's experts' reports that suggest that they approached this any differently in light of post-2020 "new science. In fact, J&J's general causation experts Diette and Merlo agreed that plaintiffs' experts did nothing new:

> Q. All right. And based upon your review of the updated reports of the plaintiff's experts—and comparing them to their reports that they also prepared back in 2018—you understand that those experts also employed the same methodology?
>
> A. It seemed—it seemed so to me. I didn't see any, you know, fundamental differences in the methodology.[205]

But now the shoe is on the other foot. Plaintiffs' experts fully embrace the statistically significant results of an association of both O'Brien 2020 and O'Brien 2024 (as well as Woolen 2022 and Davis 2022). According to plaintiffs (and the study authors), these results prove consistent. Instead of doing the same, J&J and

[205] Ex. 76, Deposition of Gregory Diette, MD at 31:11–34:13.

its experts now want to ignore the statistically significant results of O'Brien 202 and O'Brien 2024 studies and promote only the (barely) non- significant ones.

C. Dose-response relationship: New post-2020 cohort study evidence strengthens this finding, while J&J has no new scientific evidence to the contrary.

Defendants argue that evidence relating to the "dose-response relationship" factor is "sorely lacking" in the literature. (Mem. 64–71.) But as with other challenges, Defendants' argument is largely recycled attacks on a finding that Judge Wolfson already made. Therefore, it is not based on "new science" that "directly contradict[s]" her existing findings, Court's Order, ECF No. 32133, at 6, and it should be rejected.

Defendants cite to three categories of evidence: (1) epidemiologic studies that all predated 2020 and have already been admitted;[206] (2) a ten-year-old letter from FDA regarding a citizen's petition that doesn't discuss new science;[207] and, (3) a 2024 PDQ which J&J implies represents the views of the NCI, but which specifically states it "does not represent a policy statement of NCI or the National Institutes of Health (NIH)."[208]

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[206] Mem. 67 n.164 (citing Terry 2013, which was discussed by Judge Wolfson at 509 F. Supp. 3d at 176–79); Mem. 68 n.167 (citing Taher 2019, discussed by Judge Wolfson at 509 F. Supp. 3d at 163 n.36); Mem. 68, 70 (Mills 2004); Mem. 69 n.169 (citing Berge 2018, discussed by Judge Wolfson at 509 F. Supp. 3d at 163 n.36); Mem. 70, n.172 (citing Cook 1997 and Rosenblatt 2022).
[207] Mem. 64 n.160.
[208] *Id*.

However, J&J simply ignores epidemiology studies that support dose response. One such study is O'Brien 2024, describing the Sister Study cohort. In addition to the overall statistically significant increased risk of ovarian cancer with ever used of talcum powder of 1.82 (or 82% increased risk), the authors looked at dose-response from the perspective of frequency and long term use. Frequent users had a 82% increased risk while long term users had a 100% increased risk compared to sometimes users (18%) and short term users (17%).[209] As summarized by the NIH, this study showed a "persistent positive association between genital talc use and ovarian cancer, *with the strongest associations observed for frequent and long term users* and for use during reproductive years."[210] That is evidence of a dose-response relationship. It is worthwhile to note that each of the bellwether plaintiffs were frequent, long-term users, applying Defendants' products to their genital area nearly daily for decades.

Another post-2020 study that J&J doesn't discuss with respect to dose-response is Woolen 2022, whose very title was "Frequent Use of Perineal Talcum Powder Products and Ovarian Cancer." Woolen was a meta-analysis of ten case-control studies and the Nurses' Health Study cohort. The authors found that frequent use of perineal talcum powder is associated with a statistically significant

[209] Ex. 2, O'Brien 2024 at 13 and Table 3.
[210] Ex. 8 at 2 (emphasis added).

increased risk of ovarian cancer, with a pooled adjusted odds ratio of 1.47 (95% CI 1.31, 1.65).[211]

Plaintiffs' experts do not "concede that the dose-response factor is not satisfied." (Mem. 65.) Rather, Plaintiffs' experts rely on these post-2020 studies, as well as the existing literature already reviewed by Judge Wolfson, to support the dose-response relationship factor.[212]

D. Biological plausibility: post-2020 evidence further strengthens this factor.

As Judge Wolfson noted, the "biological plausibility" factor considers whether "the purported association [is] biologically plausible and consistent with existing scientific knowledge."[213] It "does not require certainty or even proof for the biological mechanism in question—the relevant question is 'whether the hypothesized causal link is credible in light of what is known from science and medicine about the human body and the potentially offending agent.'"[214]

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[211] Ex. 4, Woolen 2022.
[212] Ex. 55, Cote Rep. 27; Ex. 64, Clarke-Pearson 3d Am. Rep. 13; Ex. 54, Harlow Rep. Addendum at 2; Ex. 47, McTiernan 3d Am. Rep. 24-25; Ex. 63, Moorman 2d Supp. Rep. 4, 10; Ex. 49, Siemiatycki 3d Am. Rep. 72, 76, 78; Ex. 58, Singh 2d Supp. Rep. 1, 3, 5, 6; Ex. 51, Smith-Bindman 3d Am. Rep. 37; Ex. 65, Wolf 3d Am. Rep. 19.
[213] 509 F. Supp. 3d at 172.
[214] *Id.* at 174 (*citing Milward v. Acuity Specialty Prods. Grp., Inc.*, 639 F.3d 11, 25 (1st Cir. 2011)).

Since 2020, the plausibility of talcum powder (and whatever contaminants are contained in it) migrating through the genital tract and causing inflammation and oxidative stress continues to be specifically acknowledged in the literature. A couple of examples in the post-2020 peer-reviewed literature that strengthen Judge Wolfson's conclusion for "biologic plausibility" between genital talc and ovarian cancer are:

- **O'Brien 2020.** "By irritating epithelial ovarian tissue or fallopian tubes directly, powder could induce an inflammatory response even in the absence of asbestos. This could set off a cascade of increased oxidative stress levels, DNA damage, and cell division, all of which could contribute to carcinogenesis."[215]

- **O'Brien 2021.** "Talc applied to underwear, sanitary napkins, diaphragms, or directly to the perineal region can enter the vagina and travel up the reproductive tract. Talc particles may act as irritants, inciting an inflammatory response . . . . Additional or more severe adverse effects could occur if the talc contained asbestos, a known carcinogen sometimes mined in the same locations as talc. The epidemiologic literature supports a possible positive association between genital talc use and ovarian cancer . . . ."[216]

- **Sanchez-Prieto.** "Another example of an inflammatory factor involved in the carcinogenesis of OvCa is the use of talcum powder in the genital area. Talc, along with associated components such as asbestos or quartz, which are known carcinogens and can contaminate talc products, might ascend through the genital tract and irritate the epithelial lining of the

[215] Ex. 1, O'Brien 2020, at 56 (citations omitted).
[216] Ex. 78, O'Brien, *The association between douching, genital talc use, and the risk of prevalent and incident cervical cancer*, 11 Sci. Rep. 14836 (2021), at 2.

fallopian tubes or ovaries. This could possibly trigger an inflammatory response that may promote carcinogenesis."[217]

- **Ogunina.** "Talc is a poorly soluble particle, and animal models have shown that once deposited onto epithelial cells, it can cause chronic inflammation, leading to a series of mutagenic events, and this effect is worse in talc contaminated with asbestos, a known carcinogen."[218]

Thus, the post-2020 literature provides additional support that the talc/ovarian cancer association is plausible.

J&J does not mention any of this new science in its memorandum, and its main argument is essentially a fallacy that Judge Wolfson reversed the burden of proof, requiring J&J to disprove biological plausibility. (Mem. 71–72.) That is not what she did in her analysis. Judge Wolfson actually found that the Court had already found that the "Plaintiffs' experts provided a solid basis for their theory" "based on scientific research and reasoning." *In re J&J*, 509 F. Supp. 3d at 175. Clearly, the Court did not presume that the plausibility evidence was reliable and did not shift the burden onto J&J.

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[217] Ex. 77, Manuel Sanchez-Prieto, et al., *Etiopathogenisis of ovarian cancer: An inflamm-aging Entity?*, 42 Gyn. Onc. Reports 101018, at 3 (2022) (citations omitted).

[218] Ex. 67, Ogunsina 2023, at 1; *see also* Ex. 10, Phung 2022. Not only do the authors call talc use a "well established risk factor" for ovarian cancer, they note that the inflammation mechanism is plausible, stating: "inflammation has been proposed as a possible biologic mechanism for talc's association with ovarian cancer."

CONCLUSION

No sooner had the ink dried on Chief Judge Wolfson's 2020 *Daubert* opinion, did J&J begin to lay the groundwork for its undoing. As if repeating it over and over would make it so, it has maintained in the Court and elsewhere that "new science" had proven both this Court, *every* court, and Plaintiffs' experts wrong.

Yet the record is clear: since 2020, the work of scientists like those at the NIH, and public health authorities like Health Canada, EPA, and IARC, continued. And that work uncovered the very evidence J&J said was lacking and proves Plaintiffs' point: that Johnson and Johnson's talcum powder products—whether laced with asbestos or not—can cause epithelial ovarian cancer.

For the above stated reasons, the Plaintiffs' Steering Committee respectfully requests that the Court deny J&J's motion to revisit and vacate Chief Judge Wolfson's 2020 order.

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